DESIGNING TANGIBLE TABLETOP INTERACTIONS TO SUPPORT THE FITTING PROCESS IN MODELING BIOLOGICAL SYSTEMS

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DESIGNING TANGIBLE TABLETOP INTERACTIONS TO SUPPORT THE FITTING PROCESS IN MODELING BIOLOGICAL SYSTEMS

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SUMMARY

This thesis aims to explore how to physically interact with computational models on an interactive tabletop display. The research began with the design and implementation of several prototype systems. The research of the prototype systems showed that tangible interactions on interactive tabletops have the potential to be more effective on some tasks than traditional interfaces that use screen displays, keyboards and mice. The prototype work shaped the research to focus on the effectiveness of adopting tangible interactions on interactive tabletops.

To substantiate the thesis claims, this thesis develops an interactive tabletop application, Pathways, to support the fitting process in modeling biological systems. Pathways supports the concepts of Tangible User Interfaces (TUIs) and tabletop visualizations. It realizes real-time simulation of models and provides comparisons of simulation results with experimental data on the tabletop. It also visualizes the simulation of the model with animations. In addition to that, Pathways introduces a new visualization to help systems biologists quickly compare the simulation results.

This thesis provides the quantitative and qualitative evaluation results of Pathways. The evidence showed that using tangible interactions to control numerical values is practical. The results also showed that in experimental conditions users achieved better fitting results and faster fitting results on Pathways than the control group, which used the systems biologists' current tools. The results further suggested that it is possible to recruit non-experts to perform the fitting tasks that are usually done by professional systems biologists.

1 INTRODUCTION

Before electronic computer technologies provided fascinating graphics and powerful tools to compute complex problems, people used mechanical computing devices and physical models to solve these problems. Chemists and science teachers used reconfigurable chemical models to explain molecular structures. In 1953, Watson and Crick presented their double helix structure of DNA using a physical model [Watson and Crick 1953], whose structure was difficult to illustrate with a mere paper drawing. Engineers used slide rules to calculate. Ancient people used abacuses for calculation in their daily life. These tools provided simple kinesthetic interaction that everyone has learned from everyday experience, e.g. grasping and moving objects. A kinesthetic interaction that embodies the computational behavior in the real world helps people understand complex spatial relationships and solve complex problems, e.g. combining two molecules to create another molecule using physical models to resemble the real world chemical reaction and moving beads in an abacus to count numbers.

I want to start with a puzzle-solving computer game that demonstrates spatial relationship of problems on screen. In 2010, Foldit, an online protein solving computer game, attracted a great deal of attention [Cooper et al. 2010]. While most of the attention focused on the citizen science aspect, I found Foldit interesting because of its kinesthetic interaction. A central component of the success of Foldit was its direct manipulation interface, which allows players to grasp, pull, move, and twist protein strands from different 3D perspectives as shown in Figure 1-1. This interface showed that the change in the interaction and presentation changes how people can think about problems, making it possible for a teenager or other non-scientists to be able to solve a complex protein folding problem because the control and presentation of the problem has been changed to something that becomes accessible to their senses in a kinesthetic way – they can now manipulate the protein strands and immediately see the results. Protein folding is a spatial/structural problem, and the Foldit game leveraged this to create an interface that connected the spatial/structural features of the problem with the actions that users could perform to solve the problem. Foldit connects the users' mental model of the problem with the representation they perceive and the actions they perform on it. It integrates kinesthetic interaction with digital media.

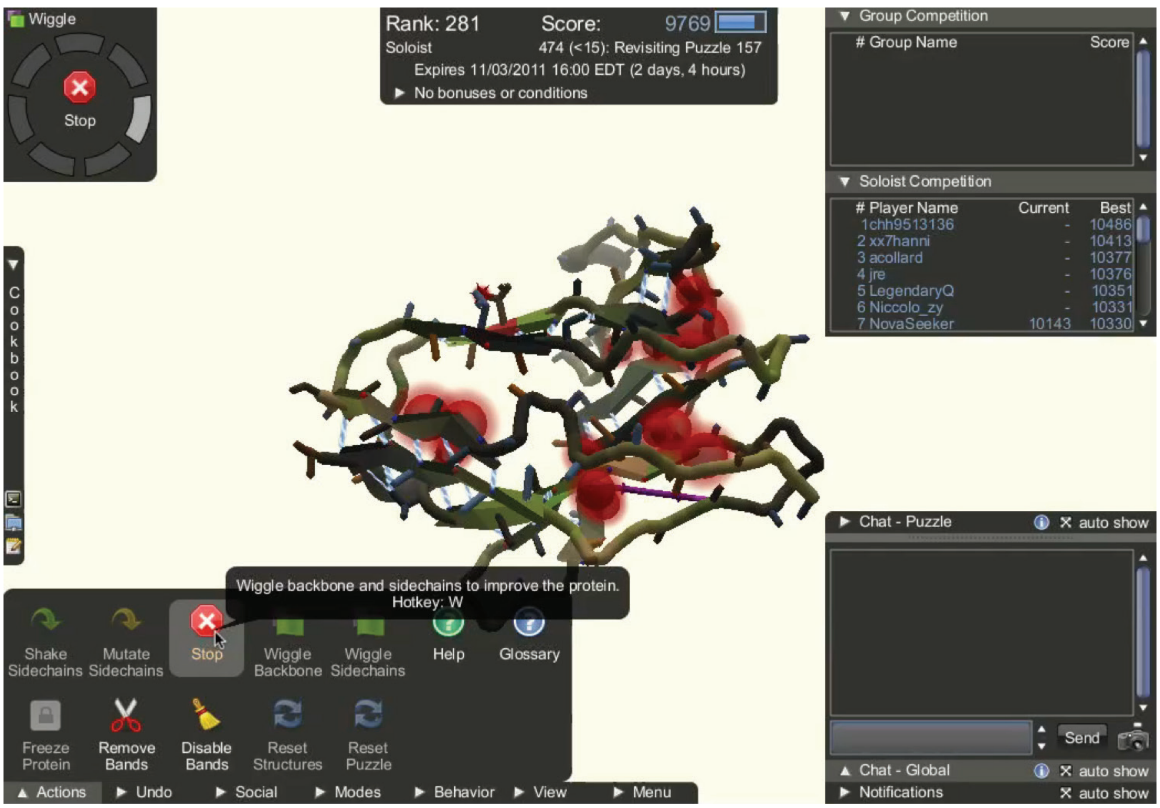


Figure 1-1 The Foldit interface. (Image captured from the game interface)

Foldit's approach of kinesthetic interaction works because there is a connection between perceptual representations (the protein structures a user sees on the screen), motor representations (the user's hand actions of controlling the mouse and keyboard to directly manipulate the protein structure), and the cognitive representation (the imaginary protein structures in the user's mind). In other words, there is a shared representation (a common code) for perception, action, and cognition [Hommel et al. 2001; Decety 2002; Prinz 2005]. Foldit provides users kinesthetic control over visual elements, allowing players to manipulate protein strands. Foldit uses keyboards and mice to manipulate protein strands on a graphical interface, but the direct manipulation of the protein strands provides kinesthetic interaction, which is a central factor to the success of the game - it allows the motor system to work closely with the visual and imagination systems while it helps solve spatial problems.

The advent of computation has opened a new realm of science that lets us tackle a broader range of problems and also more complex problems, but it has the downside of black boxing large parts of the processes which are not well understood by the scientists. At the same time, tangible interaction is a new paradigm for how we can interact with digital information. For example, toy blocks and other construction toys help children develop motor skills, spatial skills, and creative problem solving skills. Interaction technologies have augmented this constructionist approach. Resnick's Programming Bricks [Resnick et al. 1996] gives users the power to create physical constructions and control them with modular sensors, motors, and computer commands.

This transition to a more embodied style of interaction with digital media has been seen broadly. In the 70s and 80s, video game controllers were mostly buttons, gamepads, and joysticks. Later, new arcade systems made use of guns to shoot enemies, steering wheels to drive race cars, or even the user's own body to control a skateboard. In 2006, the Wii Remote, a more embodied controller with motion sensors and an infrared camera, changed the game controller. With the added sensors in the controller, Wii Remotes became able to detect more complicated arm movements of the players. Instead of using fingers to press buttons, users of the Wii Remote could use their bodies to control the virtual avatars on the screen by holding the Wii Remote in their hands. Therefore, a player could swing the Wii Remote the same way she swung a tennis racket. The Wii Remote introduced a human computer interaction that was more natural than using conventional keyboards and mice. More recently, the Kinect has brought full body interaction to the game. With a Kinect, users do not need to hold any controllers. They use their bodies and gestures to interact with the virtual world. This transition is also seen from desktop computing to mobile, tablet, and tabletop computing. The interface has transitioned from monitors, keyboards, and mice to interactive surfaces and tangible user interfaces. Interactive tabletop displays further support spatial applications. The table senses the movements of manipulable objects placed on the tabletop. The tabletop display provides the visual feedback for the objects. And importantly, the feedback can be spatially co-located with the objects or with the touches in the case of a touch-sensitive display. Typing, clicking, and moving a mouse are all remote actions, and there is no visual feedback that is spatially coupled/co-located with them. Unlike with typing, when clicking or moving a mouse around on a computer, users have to move their bodies to different locations not only to control the tangibles on the tabletop but also to read the visual output from different angles.

Cognitive researchers argue that building physical models and computational models in scientific activities contributes to innovation [Nersessian and Chandrasekharan 2009]. Cognitive scientists have further studied the role of using external artifacts in problem solving [Alac and Hutchins 2004; Hutchins 1995; Hutchins and Lintern 1995; Chandrasekharan 2009]. Because of the recent evidence in cognitive science mentioned above, it is worthwhile to embody computational simulations. The success of Foldit shows how the interconnections between perceptual, motor, and cognitive systems can be used to discover novel protein folds, as the visual representation on the screen allows users to determine a protein shape by exploring its structure from different angles and by experimentally twisting and pulling on it. A big advantage of such kinesthetic interaction is that embodied interfaces necessarily have movement properties and can enable the creation of complex and fine-grained movement patterns. It seems worthwhile to embody our interactions by using a physical interface with computational simulation. Extending this interaction to physical space with a Tangible User Interface (TUI) can enhance comprehension and learning. However, representing abstract and numerically complex scientific problems using tangible interfaces remains a challenge.

1.1 Basic Concepts and Approach

The evidence presented in the previous section shows that physical objects augmented with digital media can make people look at things differently and they might also stimulate creative solutions and discoveries. This type of interaction can be beneficial to education or even help bring about scientific discovery. My vision of this type of interface should happen in a three-dimensional physical space, where a physical object has context-aware capability and gives the user appropriate feedback visually or through other senses. The concept is similar to the idea of radical atoms [Ishii et al. 2012] proposed by Ishii. However, fully realizing this three-dimensional type of interface is difficult with available technology. Therefore, I have attempted to realize this concept on a two-dimensional horizontal interactive surface, specifically an interactive tabletop display.

The research goal of this thesis is to explore how to physically embody and interact with computational simulations that have spatial and temporal properties on an interactive tabletop display. The research approach consists of three stages. The first stage involved the construction of interactive tabletop displays [Mazalek et al. 2009b] to be used in later research. In this stage, my collaborators and I evaluated several different types of interactive tabletop prototypes, including Frustrated Total Internal Reflection (FTIR), Diffused Illumination (DI) and a combination of both. Finally, we overcame the physical limitation of the equipment and designed two 60” interactive tabletop displays. The process literature review continued until recently as my research on tangible interaction became broader.

The second stage explored methods for tangible interaction on an interactive tabletop display. In this stage, I participated in the InSpace project [Reilly et al. 2010] and helped develop several different types of tangible controllers for mixed reality office space. I also designed tangible interactions utilizing physical objects on an interactive tabletop display [Wu et al. 2011a]. We experimented with different techniques, such as Radio-Frequency Identification (RFID) and computer vision and laser tracking to track objects in an office space. We found several challenges designing a collaborative virtual environment. We also proposed several possible solutions to resolve the challenges. I also joined several other projects and designed tabletop interactions using fingers, objects, pens and smartphones.

The third stage was to refine my research questions and design studies to answer the questions and support my hypotheses. After exploring different techniques and interaction designs, I started to look at cases where TUIs can be more effective than non-TUIs. One science simulation game, Optical Chess, caught my attention, as it was a newly designed game that was available only with GUI. To demonstrate that TUI improves the way we think and solve problems, I built a tangible version of it, Tangible Optical Chess [Wu et al. 2010], to show that players of TUI games develop more strategies than players of GUI games.

In the third stage, to verify the concept that tangible interaction improves the way we think about and solve problems in computational simulations, I collaborated with systems biologists from the Biomedical Medical Engineering (BME) department. Based on the ethnographic research of my collaborators, we identified several problems faced by modelers in a systems biology lab. Their current modeling approach, which is to sketch the model and manually create programs to generate simulation results that fit the experiment data, does not give the modelers a clear way to look at the problem since the feedback from the simulation does not relate to the action they perform on the model. To illustrate that TUI has the potential to solve these modeling difficulties, I built a prototype of a biomedical simulation application, Kinesthetic Pathways, [Wu et al. 2011b] on an interactive tabletop display to show that kinesthetic interaction can help users resolve complex modeling problems. I also designed an experiment to prove my thesis claims with statistical quantitative data and subjective qualitative feedback.

1.2 Thesis Statement

Tangible interactions with appropriate visual feedback on an interactive tabletop display surface can provide an effective means for representing and controlling computational simulations such as scientific models.

In the context of this thesis, appropriate visual feedback means visual feedback on the tabletop that contributes to controlling and understanding the computational model. "Effective means" denotes that a tangible user interface provides desired and intended feedback that contributes to the user's ability to solve the problem faster and better. This thesis focuses on the tangible interaction on an interactive tabletop display. The interactive tabletop display provides the visualization capability to enhance the tangible interaction and complements the insufficient visual feedback of a simple physical object on the tabletop. In a scientific simulation application on an interactive tabletop, a user can embody the simulation and obtain immediate feedback from the tabletop. This thesis will present an interactive tabletop application developed to make the fitting process in biomedical modeling more effective. I will show statistical evidence and subjective user feedback to support my thesis claims.

1.3 Thesis Contributions

In supporting the thesis statement, this dissertation makes a number of specific contributions.

1. A new fitting approach that employs tabletop tangible interactions with visual feedback

Fitting is the process a systems biologist uses to compare the simulation results with the experimental data and decide the next step of modeling. According to one systems biologist I work with, this process is not scientific. It is a process that requires intuition and some luck. Even though systems biologists adopt computational methods to optimize the solution, they often do not see the activities of optimization and do not understand the process. The new proposed tangible interaction-based fitting process allows systems biologists to perform the fitting task with the help of tangible interaction and visualization.

2. Evidence to support the use of tangible tabletop interaction in modeling biological systems

Pathways visualizes the simulation of bio-chemical networks using a TUI approach. In current tools in systems biology, researchers run simulation programs that model different experimental parameters such as concentrations inside molecules and reaction speeds. These parameters are adjusted to discover hidden patterns in the reaction network, often using graphs to plot the output. I believe that by adopting TUIs for visualization, researchers will be able to manipulate these parameters more easily and also see the system-wide effects of their manipulation across the reaction network. My first attempt was to visualize the reaction network on an interactive tabletop display. Researchers control the parameters with tangible objects and their hands, allowing the objects to change parameters in a continuous fashion, which focused the researchers' attention on understanding the effects of this manipulation, rather than on programming or entering numerical values.

To support my thesis statement, I designed an experiment to compare the efficiency between Pathways and the systems biologists' current tools. The experiment was a within subject design that included systems biologists and regular users. The results showed that when using Pathways for the fitting process, modelers could obtain better solutions (the simulation result is closer to the experimental data) and faster ones (finding a satisfying solution in a shorter time) than those completed with the systems biologists' current tools. The user evaluation also shows that the tangible fitting method is more effective than the systems biologists' current tools. Moreover, the evaluation results suggested that on Pathways, non-experts could complete the fitting tasks as good as experts.

3. **Design and development of large interactive tabletop displays to foster research projects**

To demonstrate my idea of tangible user interface augmented with visualization, I need a platform that can support this feature. An interactive tabletop display that has the capability to identify the location and orientation of an object on its tabletop is an ideal platform to realize this concept. Moreover, constructing these interactive tabletop displays also contribute to the development of other projects in the research lab. During my research, I have constructed three interactive tabletop displays with different sensing technologies and slightly different designs.

4. Remediation of a GUI-based game to tangible tabletop and observation of effects (Optical Chess)

The comparison between the two interfaces of Optical Chess allowed me to demonstrate that people strategize better with the TUI than with the GUI. Optical Chess is a chess-like strategy game invented by my collaborator, David Joyner [Joyner et al. 2009]. We created a tangible tabletop version of it. Players can come to the table, pick up the delicate physical chess pieces, and start playing the game. Observing the playing of the two versions of optical chess suggested that the tangible user interface (TUI) allowed users to develop more strategies than they would with a GUI. This discovery was consistent with the movement of user interface development and made me confident that I should concentrate on inventing tangible interaction for my later projects. As a result, I created Pathways to tackle more complex computational models.

1.4 Thesis Overview

The following chapter considers the conceptual foundations underlying the development of my thesis. The chapter begins with tangible interaction theories from different perspectives and then provides an overview of relevant cognitive science frameworks. It next considers the development of interactive tables and concludes with a discussion of design principles in information visualization.

Chapter 3 presents research projects relevant to my work and the inspiration I gained from them. The chapter starts with a discussion of tangible interactions on interactive tabletops. After that, it shows scientific simulations that I investigated when I designed the Pathways prototype on the tabletop. TUI-based visualizations are also considered before the chapter concludes.

Chapter 4 presents the supporting work that I developed prior to Pathways. It illustrates Tangible Tracking Tables, interactive tabletop displays I constructed to develop several other applications. It also presents Tangible Optical Chess, a tangible tabletop strategy game. The end of this chapter compares the evaluation results of the GUI and TUI versions of optical chess.

Chapter 5 presents the development of Pathways. It starts with an introduction of practices in a systems biology lab. Then, the chapter describes the iterative design of Pathways. After that, it designates the simulation method, visualization, and the tangible interaction of Pathways.

Chapter 6 presents an experimental evaluation of Pathways by presenting both qualitative and quantitative data to support my thesis. The evaluation results show that Pathways provides a more effective interface for the fitting process than do the systems biologists' current tools.

Finally, Chapter 7 presents a more subjective discussion of the impact of Pathways, its potential applications, and the future work.

The Appendix includes the construction plan of the tangible tracking table, the API specification of Pathways, the IRB protocol, and the experiment guide.

2 Conceptual Foundations

This chapter summarizes the theoretical foundations that support my research. They are the tangible interaction theories, the cognitive science, interactive tabletop and visualizations.

2.1 Tangible Interaction Theories

Research of tangible user interfaces has become a hot topic in HCI. There are several different theories that try to explain why tangible interaction works. Some of the noticeable frameworks emphasize different views for the design of tangible interaction [Hornecker and Buur 2006].

The *data-centered view* [Dourish 2004; Ullmer and Ishii 2000] sees tangibility as based on the coupling of digital and physical media. These researchers propose that Tangible User Interface utilizes physical representation of objects and manipulates digital information that couples with the physical artifacts. Mazalek illustrates this concept with examples of bottles [Mazalek et al. 2001]. Ullmer [Ullmer 2002; Ullmer et al. 1998; Ullmer et al. 2003] further showed through experiments that TUI is faster than GUI for a range of simple querying tasks. From the perspective of the *data-centered view*, the key characteristics of TUI are that physical representations are computationally coupled to underlying digital information, physical representations embody mechanisms for interactive control, physical representations are perceptually coupled to actively mediated digital representations, and that the physical state of interface artifacts partially embodies the digital state of the system [Ullmer and Ishii 2000].

Researchers from arts and architecture [Bongers 2002] proposed another view, the *space-centered view,* to explain that TUI uses examples of physical objects in interactive spaces. Hornecker et al. [Hornecker and Buur 2006] also introduced a framework for designing tangible interaction for social interaction in physical space. Interactive installations and spaces rely on combining physical space and objects with displays [Lee et al. 2008; Rydarowski et al. 2008], wind, or sound feedback. Full-body interaction [Samanci et al. 2007] and using part of the body as an input device are also fit into this approach.

In 2008, Fernaeus et al. [Fernaeus et al. 2008] defined a tangible object as a resource for multiple kinds of actions from an *action-centric view*, which saw a tangible artifact work as a resource for multiple kinds of actions. They suggested that the definitions of tangible interfaces should put more value on human action and less on the representation and transformation of information. In this view, a tangible artifact can allow physical manipulation by the user. It can also provide perception and sensory experience. A tangible artifact has the potential to make references to itself or be passed to other people. Moreover, a tangible artifact usually provides rich digital media with it as well.

The *perceptual-motor-centered view* is another perspective that emphasizes that feedforward and inherent feedback are two criteria for good tangible interface design. [Djajadiningrat et al. 2002; Djajadiningrat et al. 2004] A tangible design takes behavior and action as its starting point. Affordances of the tangible interface have relevance only in relation to what we can perceive and what we can do with our body. In this approach, perceptual and bodily skills are highly important, and tangible interaction is therefore a logical conclusion.

Ishii has further proposes the concept of Radical Atoms [Ishii et al. 2012]. The notion of Radical Atoms is based on some extremely malleable, and dynamic physical materials that are mutually coupled with underlying digital information so that dynamic changes of the physical form can be reflected in the digital states in real time, and vice-versa. Ishii thinks Radical Atoms should fulfill three requirements. It transforms its shape to reflect the underlying digital information and user input, e.g. the Tangible Pixels [Gross and Green 2012]. It conforms to the constraints of the physical environment and user input [Patten and Ishii 2007]. Finally, it informs the user of its dynamic affordances as well [Lee et al. 2011].

Even though researchers try to define tangibility from multiple perspectives, these different views share one common characteristic, which is the coupling of digital media and physical objects.

2.2 Cognitive Science

In this thesis, TUIs are external representations directly perceivable by the human senses, including the visual and tactile senses. The role of external representations has received attention by cognitive scientists who are particularly interested in the Distributed Cognition (DC) framework. Some of these scientists focus on the use of external representations [Hutchins 1995; Hutchins and Lintern 1995], while others concentrate on the processes of generating representations [Chandrasekharan and Nersessian 2011; Nersessian and Chandrasekharan 2009]. The DC framework describes the roles of physical artifacts, the physical world, in supporting memory, learning, and social communications.

Common coding framework has recently been used to explain how building computational models, particularly models with dynamic visualizations, can lead to new discoveries and concepts [Chandrasekharan 2009]. The core concept of this building modeling for discovery is a coupling between the modeler's imagination and the external dynamic visualization [Nersessian 2008]. Common coding allows movements in the visualization to be replicated by the modeler's actions, and this replication allows these external movements to be integrated with the internal movements in the modeler's mental model.

Zhang and Norman designed experimental tests to find out the role of external representations by studying the Tic-Tac-Toe game and the Towers of Hanoi [Zhang and Norman 1994]. They found that by increasing the external representations, subjects had statistically significant improvement in their solution times, number of steps, and errors. Based on the experiment results, Zhang and Norman made several conclusions. First, they argued that external representations could provide memory aids, which can help users be aware of the states of the problem. Secondly, external representations can provide information that can be directly perceived and used and further provide affordances. Thirdly, external representations can anchor and structure cognitive behavior. In other words, the physical structures in external representations constrain the range of possible cognitive actions. In this thesis, the external representations are made up of tangibles and visualizations. The tangible representations are used as controls, such as a way to check pieces in a game, a dial to manipulate numerical data, or a toy figure to navigate the virtual world. The visualizations show the structure of the model, the status of the molecules, the comparison of the simulation and the experiment and provide a new graphical representation of data using the radar chart.

The original objective of Kinesthetic Pathways was to create an interface that would allow systems biologists to build models using tangible interaction on the tabletop. After that, the systems biologists could conduct the fitting process with kinesthetic tangible interactions such as rotating a dial on a selected visual element. Since there are already studies covering the building of external representations for scientific research and tools designed for solving scientific problems by creating visual representations of the problems, in this thesis, I am interested in presenting a tangible interaction to tackle the fitting process and proving its efficiency. Therefore, in the evaluation of this new tangible interaction method, subjects will face a predefined model. In other words, users will use the representation rather than create the representations. Eventually, in the finished Kinesthetic Pathways system, users will be able to create their own models.

2.3 Interactive Tabletop

Interactive tabletop displays provide a large screen area and allow multiple people to work collaboratively. They have lower technical barriers than traditional Graphical User Interfaces (GUIs), as people are familiar with the idea of working at tables, something they have done since they were young. Also, people working at a table have virtually the same access to any spot on the table. Scott et al. [Scott et al. 2000] pointed out several major benefits of using tabletop interfaces for collaborative activities. Tabletops have long provided interaction space for groups of people to share different collections of physical and informational objects. With the rapid development of computing technology, tabletops have provided capabilities to manipulate and manage a large variety of physical objects and digital media. Many interactive tabletop systems have been developed recently [Microsoft 2012; Jordà et al. 2007]. Most of them share common characteristics: they can track multiple objects and multiple finger touches, and they simultaneously project interactive information on the tabletop.

The sensing technologies of interactive tabletops are usually vision technology [Hodges et al. 2007; Jordà et al. 2007; Wilson 2005], capacitance sensors [Dietz and Leigh 2001; Patten et al. 2001] and other special hardware [Mazalek et al. 2002]. The most accessible technology among them is the vision technology. It is low cost and scalable to larger sizes of tabletops. The Tangible Tracking Table I created used computer vision to detect interaction on the tabletop surface. However, it also has some drawbacks. First, computer vision sometimes is not reliable. It is highly affected by light conditions and small vibrations of the equipment. Unlike other technologies that have dedicated chips to process the signal, computer vision technology relies mainly on a computer's CPU computing power to process the captured image. Most common cameras operate at only 30 frames per second, which is not fast enough to support high fidelity input. The sensing algorithm is usually tailored to a special task, for example, gestural sensing. Accomplishing multiple tasks at the same time costs more computing power.

2.4 Visualizations

I define visualization as the formation of a visual representation of an abstract concept. Even though computers have brought visualization to a level that other forms of visualization cannot reach, e.g. the procedural, participatory, encyclopedic, and spatial qualities of this digital medium [Murray 1997], I see Information Visualization (Infovis) as not necessarily having to happen on a computer. The procedural quality of digital media allows us to program and set up rule-based behavior for computers to repeat and follow. The participatory quality of digital media allows it to be manipulated by the users. The encyclopedic capacity allows a computer to hold more information than any other media. These qualities allow the computer to generate a spatial quality that allows users to navigate a virtual space, something that no other media can do. When we inspect the visualizations on the computer screen and the presentation work done by artists, designers, and architects, we can see the basic theories and principles such as cognitive psychology, graphic representation, and visual languages applied in all types of visualization.

Tufte's design principle [Tufte et al. 1990] covers several aspects of the visual presentation of data. Simplicity and maximizing data-ink ratio are the main ideas that interweave these design principles. Simplicity means using graphic elements efficiently, and avoiding chart junk, which is all of the visual elements in charts that do not help a viewer comprehend the information represented, for example, ink that is not associated with the data and legends on a map. Applying simplicity to tangible design implies using metaphors effectively. Tufte also believes that all designers should maximize the data that the audience can perceive with minimal ink (or pixels on the screen). In GUIs, this data-ink channel is constrained in the screen and in conventional input devices like keyboards and mice. In TUIs, non-traditional devices and new sensing technologies have created different forms of interactions - the human body interacts with the physical environment, which is directly embedded with digital information. By providing tactile feedback and embodied interaction that has a greater degree of freedom than using keyboards and mice, TUIs can exploit human perceptions and actions with machines that GUIs cannot.

Shneiderman concluded the taxonomy of information visualization tasks, which are overview, zoom, filter, details-on-demand, relate, history and extract [Shneiderman 1996]. Pathways was designed mainly to support modeling. Therefore, not all of these fundamental tasks were covered. However, during the iterative design of Pathways, I found that the systems biologists demanded some of these features. For example, some systems biologists wanted to see the ODEs of a reaction (details-on-demand); some of them wanted to compare the output of two different initial conditions (relate); when they found the previous fitting solutions were better, they wanted to roll back to a previous setup (history).

The main goal of Pathways was to make the modeling more effective for systems biologists. It was not designed to be an all-purpose information visualization tool that visualizes variety kinds of data. Therefore, some of the fundamental visualization tasks proposed by Shneiderman were not implemented in current version of Pathways. Nevertheless, designing an interface that is also educational to non-experts is another goal of Pathways. When designing Pathways, I tried to increase the data-ink ratio without distracting users. The animations and colors provide most important modeling information to users. Yet they are not distracting. Novice users can be benefitted from learning biomedical reactions on Pathways.

3 Related Work

Several research areas influence this work: interactive tabletops and the studies of the tangible interactions have shaped the interaction design of my research on tangible tabletop interaction. Scientific simulations provide examples of interfaces for manipulating scientific data. Visualizations have implications for designing the visual feedback of the tabletop application in this thesis. This chapter summarizes relevant research from each of these areas as it relates to my effort.

3.1 Tangible Interaction on Interactive Tabletops

From Ishii's perspective, interactive surfaces are considered TUIs [Ishii and Ullmer 1997]. Horizontal interactive surfaces, namely interactive tabletops, detect objects or human gestures on the tabletop (Cao et al. 2008; Jordà et al. 2007). At the same time, digital information is projected onto the tabletop to provide visual feedback.

Within the abundant applications of interactive tabletop displays, I categorize objects used on the tabletop displays into two groups: active objects and passive objects. An active object is a physical object that has an input or output gadget attached to it. The gadget can be a button, a small display, a dial, or some device that keeps sending data to the interactive tabletop. A passive object, on the other hand, is any object that does not qualify as an active object. A passive object can be a wooden cube, a toy statue, or a piece of paper. Despite the fact that no passive objects send digital data to the interactive tabletop, they should nevertheless be tagged so that they can be identified by the interactive tabletop. Some of these objects are tagged by RFID [Sengers and Gaver 2006]. Some of them are detected by electromagnetics [Patten et al. 2001]. Most recently, computer vision has played an important role in recognizing these objects by using fiducial tags (Jordà et al. 2007). When a passive object is placed on an interactive tabletop display, the display provides the complementary visual feedback. For this reason, in my thesis, I refer to all the active and passive objects on interactive tabletop displays as *responsive* objects.

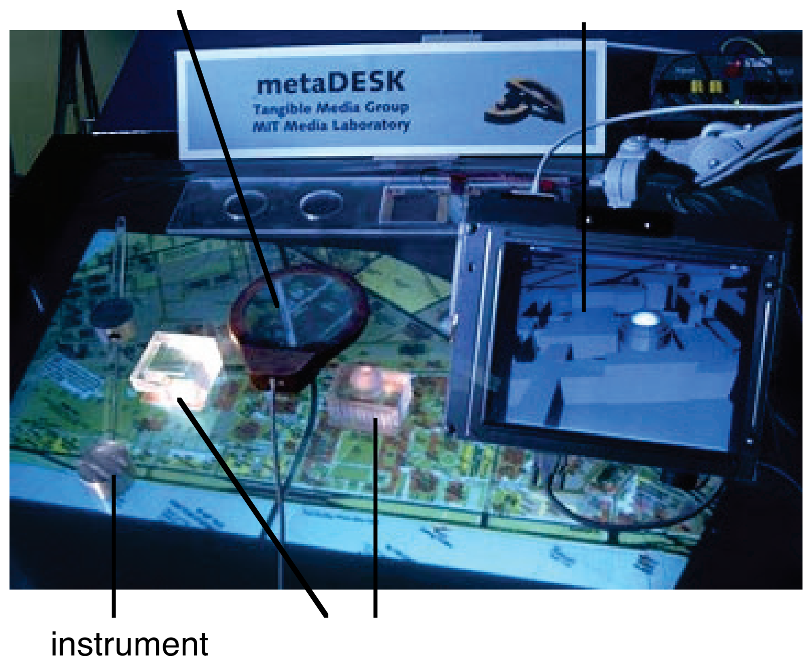


Figure 3-1 The metaDesk

MetaDesk [Ullmer and Ishii 1997] is an interactive surface that utilizes phidgets (physical widgets) as the control. In MetaDesk (see Figure 3-1), which uses both passive and active objects, a user moves an activeLENS to change the view of the virtual world. Directly controlling the camera view is a more tangible experience than sending numeric values to the system or moving a mouse to control the camera angle. Phidgets can be used to control the zooming function with some constraints. Every tangible piece in the MetaDesk maps to a corresponding GUI element (see Figure 3-1).

From the perspective of data-centric TUI design, it is important to assign an appropriate metaphor to each tool so that each object will give an indication of the function available to the users. For example, a clock allows people to make the assumption that it is related to time; the physical MIT dome model in the left photo in Figure 3-2 suggests that the phicon (physical icon) is used to locate the MIT's dome on the map. From the perspective of action-centric TUI design, affording certain actions that give meaning in the context of interaction should be taken into account. For example, the rotation constraint instrument in metaDesk (see the right photo in Figure 3-2) limits the two cylinders' movement and rotation by being connected to a sliding bar.

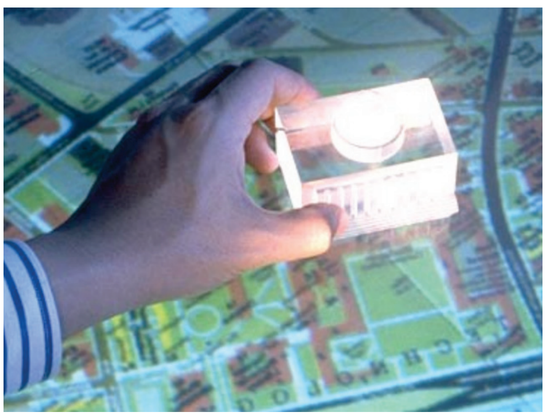


Figure 3-2 In the left photo, when a user puts an MIT dome model on the table, the scene changes to the MIT campus immediately. In the right photo, a user moves the two objects attached to a rod to demonstrate zooming. Similar zooming methods are now popular on many multi-touch interfaces with finger touches.

Several tangible user interfaces use simple metaphors such as blocks, lenses, and miniature models to represent complex systems. Urp [Underkoffler and Ishii 1999], an urban planning tabletop application, uses miniature architecture models to simulate the shadow and wind flow of a building. In this application, a user moves the tangibles of buildings on a tabletop (see Figure 3-3). The shadow of the building and the wind's magnitude and direction are projected onto the tabletop. The user controls the interface with objects directly. The objects in Urp are all passive objects with colored tags for the camera to recognize their identities, locations, and orientations. A top-down projector projects the simulated shadows, wind flows, and annotated messages onto the tabletop surface. Urp is a TUI whose visualization is directly controlled by tangible models.

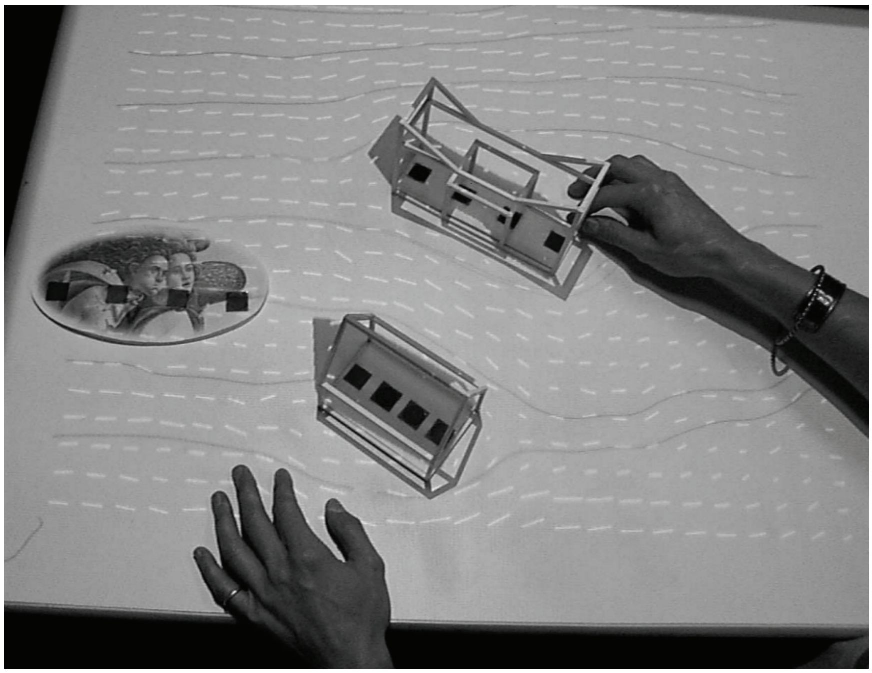


Figure 3-3 Urp, a system for urban planning.

Architales is an interactive tabletop project [Mazalek et al. 2009a] that emphasizes digital and physical co-design of interactive story tables and environments for gallery exhibition (see Figure 3-4). It is capable of tracking multiple finger touches and tagged objects, as well as recognizing several gestures. The display surface of the tabletop in Architales measures nearly 60 inches diagonally. The table uses reacTIVision [Kaltenbrunner and Bencina 2007] as its core engine to read the inputs. For the application layer, it uses Multi-touch for Java (MT4J) [Laufs et al. 2010] and processing core library as the application level framework to integrate with other programs.

Additionally, this interactive tabletop has Bluetooth and WiFi capabilities. It is also possible to be integrated with smartphones. The display of the smartphone can be a separate window in which to show dynamic information.

In recent years, many groups have developed tangible tabletop interfaces for a range of applications. An application close to our project is the use of tabletop visualization to control network models. IP Network Bench [Kobayashi et al. 2003] is based on Sensetable [Patten et al. 2001] and provides an interface for users to determine the balance between cost and performance in IP network design. Users can achieve real-time results by controlling the network model collaboratively with multiple controllers. Pico [Patten and Ishii 2007] is a TUI based tabletop surface that can track and move small objects under mechanical constraints. The position of these physical props represents and controls application variables to optimize the configuration of cellular telephone network radio towers. The computer optimizes the network, while the user moves the physical props under the constraints of other physical objects. The objects in Sensetable are passive objects that can be detected by the table through electromagnetics. The objects do not have visual outputs. A top-down projector provides the visual feedback.

Other interactive tabletops worth mentioning are Tangible Viewpoints and Tangible Spatial Narratives, which make use of tagged pawns to navigate stories on a tabletop display [Mazalek and Davenport 2003; Mazalek et al. 2002]. These projects led to the development of the TViews tabletop sensing architecture, which use active tangible objects to communicate with the table and locate the positions of the objects on the tabletop [Mazalek et al. 2006]. However, the tangible objects require complicated electronic fabrication, which is not suitable for fast prototyping. The objects are active since they continuously communicate with the table to provide accurate location and orientation information.

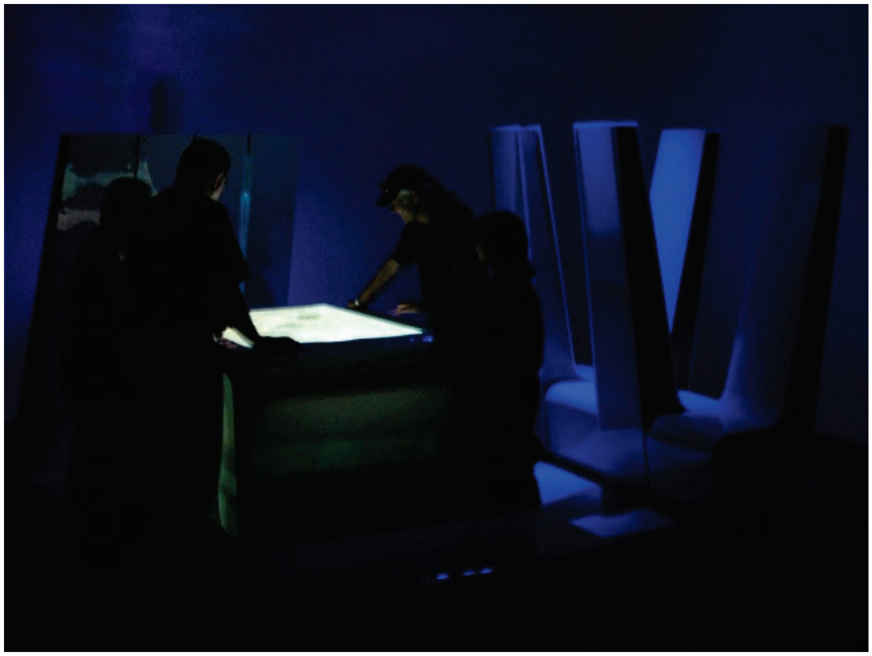


Figure 3-4 Architales

The recent proliferation of interactive tabletops has led to an explosion of possible applications. Many individual systems have been developed for experimentation, including entire frameworks dedicated to implementing board games on interactive tabletops (such as the STARS system [Magerkurth et al. 2003]) and facilitating other tabletop software (such as the reacTIVision [Kaltenbrunner and Bencina 2007]). One especially relevant project is the Illuminating Light project [Underkoffler and Ishii 1998], in which users move around various optical elements on a workspace to create different laser paths. This interface serves as an interface for optics education, letting users learn and use optical concepts in a simulated environment by allowing them to see laser paths without the need for actual lasers. Unlike Mazalek's interactive tabletop display, these tabletops use passive computer vision patterns, fiducial markers, to tag the physical objects. One benefit of using fiducial markers on these passive objects is that they are low cost and easy to create. However, the pattern recognition of the markers is easily affected by the lighting condition of the environment.

3.2 Scientific Simulation

Scientific simulations are designed to imitate the scientific rules that govern a particular field. For example, several different atomic models were proposed to simulate the orbits of electrons in an atom. Some of these models are simple but sufficient to explain a particular phenomenon. Modeling a biological system is very similar. Systems biologists have to create the model that generates the same experiment data acquired from another lab. The process, which I will describe later in Chapter 5.1, needs a lot of repetitive work. In this thesis, I present Kinesthetic Pathways, which utilizes visual representations of a model and kinesthetic interaction on an interactive tabletop to simplify the process of modeling in a systems biology lab. Kinesthetic Pathways presents the visualization of the model, the simulation results, and a radar chart that was designed to help users perform fitting tasks faster.

Sometimes scientific simulations are used for an educational or demonstration purpose. Because the purpose is to demonstrate the concept of a scientific phenomenon, these simulations usually have high-resolution 3D realistic images. However, they are less interactive than other simulation tools that allow the creation of custom simulations [Chourasia 2011; NASA 2012]. There are also more interactive simulations that allow users to change the display parameters of the visualization [Nelson 2011].

Cytoscape [Shannon et al. 2003] is a software tool for integrating bio-molecular components and their interactions with expression profiles, phenotypes, and other molecular states. It supports various automated network layout algorithms and visualizes various sizes and colors of nodes and edges. The system is extendible by adding new plug-ins, which allows rapid development of additional visualization and computational analyses. Karp [Karp et al. 2010] introduced Pathway Tools, a software environment for creating a model-organism database that can integrate the evolving understanding of the genes, proteins, metabolic network, and regulatory network of an organism. Karp supports our point that most visualization tools merely re-represent data; they don't seek to support the process of fitting data. More broadly, our objective is to help people fit data and estimate parameters. Visualizing the network is a step in that direction.

CellDesigner [Funahashi et al. 2008] is a biochemical simulation application that supports kinetic modeling. It is a structured diagram editor for drawing gene-regulatory and biochemical networks. After the user designs the structure, the system simulates the reaction and generates the results. In my interview with the systems biologists, one PhD student said of CellDesigner, "*It's one of the popular tools in the field and I didn't use it because it just doesn't suit my needs (simple models but with unknown parameter values).*" This is a common comment systems biologists give when they use other tools to help make their modeling process more effective. Because most visualization tools lack support for the fitting process, modelers usually write (their own) computer programs to simulate the reactions and models.

3.3 Visualizations

Card et al. [Card et al. 1999] define visualization as "...the use of computer-supported, interactive, visual representations of data to amplify cognition..." However, the skills of visualization or the visual representation of complicated data have been used for a very long time in other media, such as paper or walls. Other kinds of research might also not be considered traditional visualization. These present data in physical space. They exist in space in the form of interactive installations, sculptures or robots. What interests me is the tangibility of these types of visualization. These visualizations are not traditional, but they present data in a space.

Strata/ICC [Ullmer et al. 2001] in Figure 3-5 visualizes the power usage of a skyscraper by using an acrylic model of the building. The importance of this tangible user interface is it uses the physical model of a building to display data that is highly linked to the presentation of physical model. The consumption of power of every space in the building is shown directly using LEDs. Users can use a disc type of interface to change the time and see the power usage at different times.

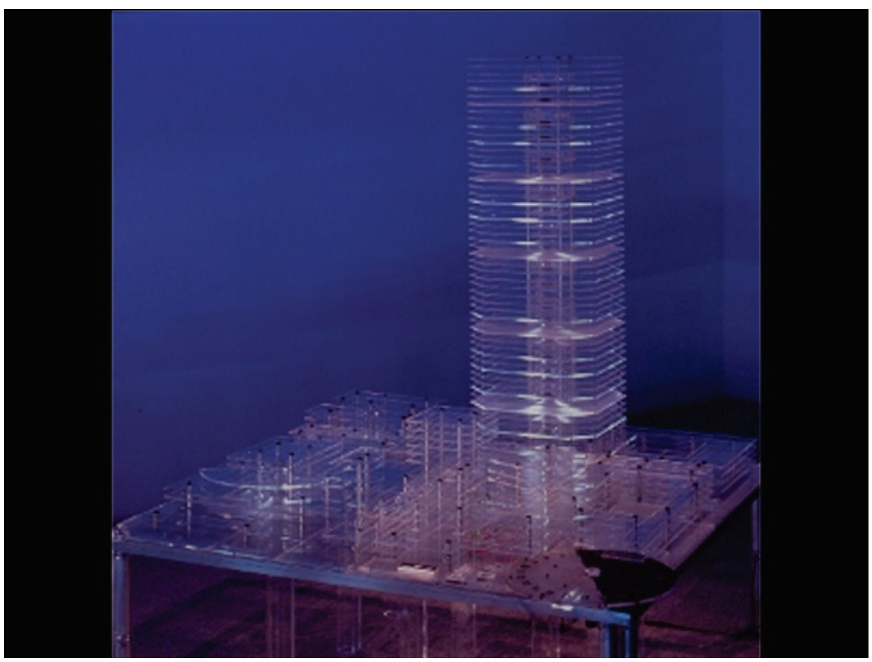


Figure 3-5 Strata/ICC. Users can control the time of the data by rotating the disc at the bottom right.

Illuminating Clay [Ishii et al. 2004] is another visualization designed in a tangible form. Instead of manipulating controllers, users directly touch and reshape the projection surface, which is made of clay. Clay plays an important role in this interface, since the clay is the controller, and the shape of the clay represents the terrain (a tactile display). Other controllers, such as physical blocks that represent buildings can be placed on the clay as shown in Figure 3-6. With the top down projection onto the clay, Illuminating Clay becomes an interface that couples digital information (projected terrain information) with physical control (clay and the model buildings).

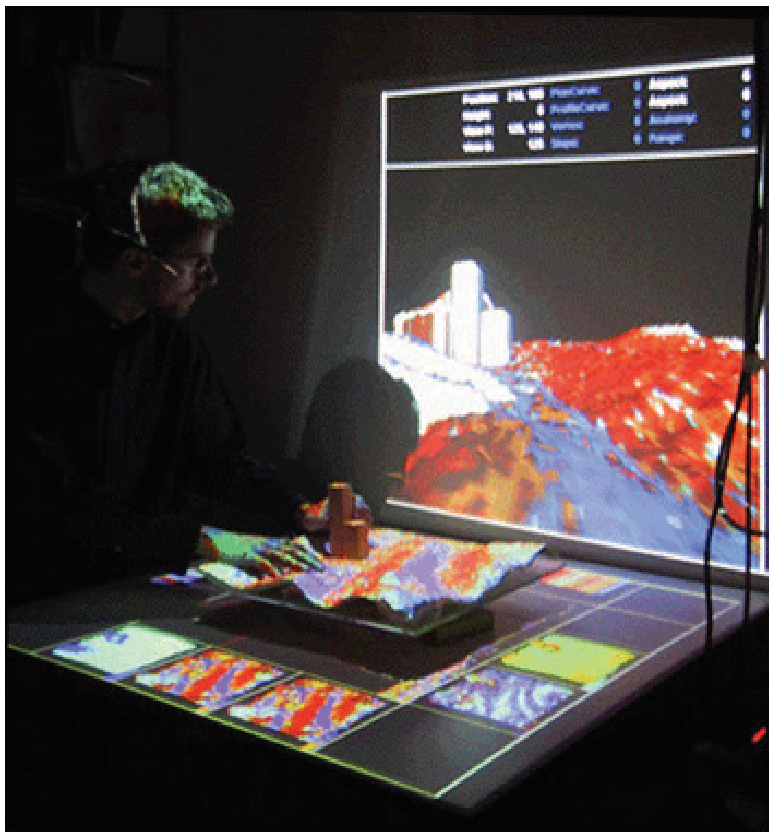


Figure 3-6 In Illuminating Clay, users touch and reshape the data with their hands

Six-forty by four-eighty [Coelho et al. 2011] is a collection of computational tiles that communicate with each other through human bodies when people touch different pieces. One tile represents simple information when it is not arranged with others. When many of them are placed together to form a pattern, they display more complicated information. Six-forty by four-eighty are screen pixels that are also responsive to touches.

Figure 3-7 Tangible Pixels adjusts their shapes to fit users' need.

Another more recent example is Tangible Pixel [Gross and Green 2012; Tang 2011], which changes the shapes and colors of furniture depending on the users' motion. When a user wants to sit down, the physical blocks form the shape of a chair to support the user's body. When a user needs a table to write, the blocks raise to the height of a table to fit the user's need. Tangible Pixel further extends interface from an object, a wall or a table to the surrounding environment. The boy in Figure 3-7 adjusts the height of the Tangible Pixels with his hands.

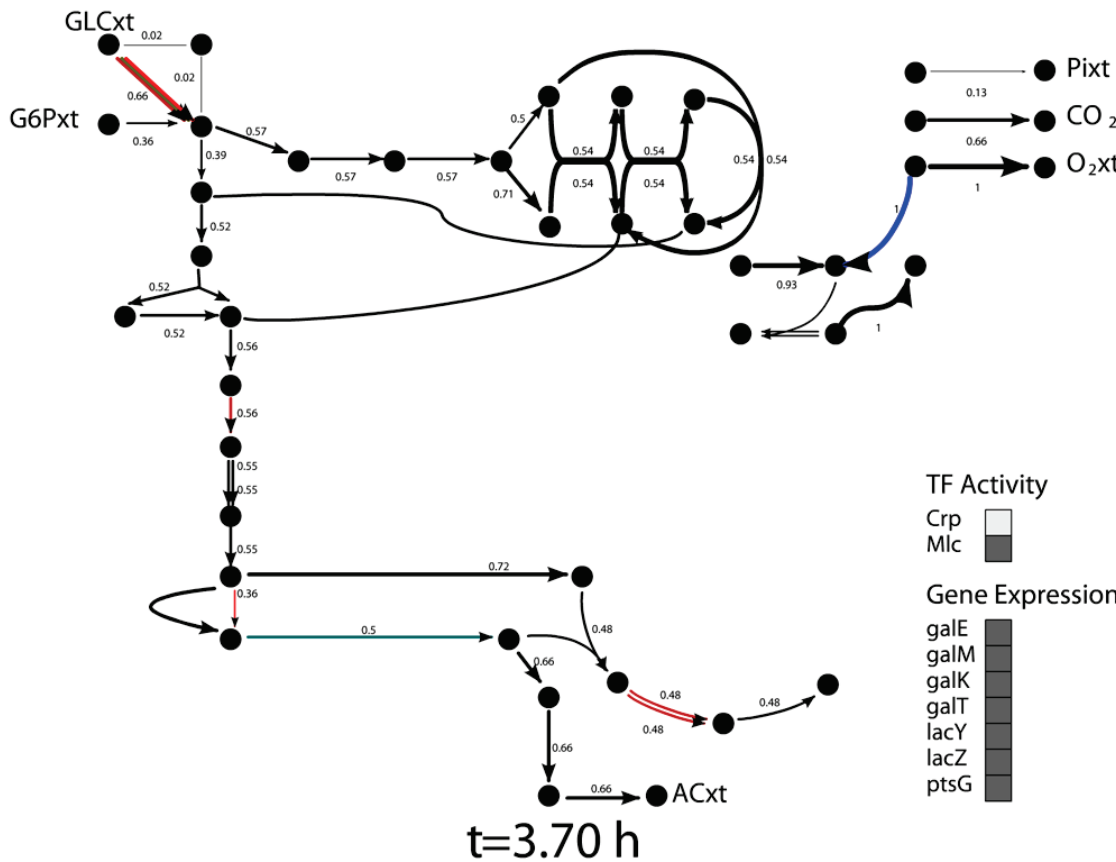


Figure 3-8 The screenshot of an iFBA model animation.

There are systems designed for visualizing biological pathways. VisANT [Hu et al. 2005] is a web-based software framework for visualizing the network models of biological interactions and relations. Users can import data from either their own data source, or from standard exchange formats. The data can be represented with millions of edges and nodes. The system not only provides analytical tools for extracting topological properties, but also supports customizing and modifying the network with user-defined sets. Another visualizing and modeling tool, Integrated Flux-Balance Analysis (iFBA)

[Covert et al. 2008] has an advantage over traditional sets of ODEs in that its flux balance models allow for analysis of the entire metabolic and regulatory network. It also has the advantage over ODE models of being able to capture intracellular concentrations and short time-scale dynamics. The iFBA approach has the potential to incorporate the advantages of both perspectives. Figure 3-8 shows the animation of iFBA model of Escherichia coli.

My vision of interface in the future is with physical objects augmented with digital/analog information in the physical space. From the related work shown in this chapter utilize tabletop, interactive surfaces, and responsive objects. In addition, the last example, the researchers of iFBA model uses animation to show a series of biochemical reactions. All of these inspired me to create applications to combine the advantages of tangible interface and traditional screen visualization. As a result, designing tangible interactions on an interactive tabletop display has become a reasonable choice to realize my ideas.

4 Pilot Work

This chapter is composed of two parts, the Tangible Tracking Table and Tangible Optical Chess. These two parts cover three stages of my research. The first stage of my research involved a literature review shown in the previous chapter and the construction of interactive tabletop displays, which will be presented in 4.1 Tangible Tracking Table. The second stage of my research explored methods for tangible interaction on an interactive tabletop display. I participated in several tabletop related projects in the Synaesthetic Media Lab (Synlab). I will illustrate some of these projects in the first part of this chapter as one of my thesis contributions. The third stage was to refine my research questions and design studies to answer the questions and support my hypotheses. The main pilot work in this stage is the Tangible Optical Chess, which is presented in the second part of this chapter, 4.2 Tangible Optical Chess.

4.1 Tangible Tracking Table

Tables have provided convenient work places for individuals or collaborative workers (e.g. a meeting table), pleasant environments for people to play games (e.g. a chess table) or a comfortable space for social activities (e.g. a coffee table). Since we are in a digital era, we are interested in the idea of bringing digital media and interactive technologies to tables to extend possibilities of tabletop applications. An interactive tabletop not only has the display capability of a regular screen but also makes objects on the tabletop interactive. Therefore, to support my research, which is largely related to tangible user interface and visualization, I designed two 60-inch interactive tabletop displays, the Tangible Tracking Table (TTT) [Mazalek et al. 2009b]. The TTT is an interactive tabletop display that can track multiple objects and finger touches at the same time. The TTT includes the software design and hardware construction of an interactive table. The software design is based on the Responsive Objects Surfaces and Spaces (ROSS) API project [Wu et al. 2012], which is a cross-platform software infrastructure that helps to manage multiple layers of communications between applications and tangible devices.

4.1.1 Design

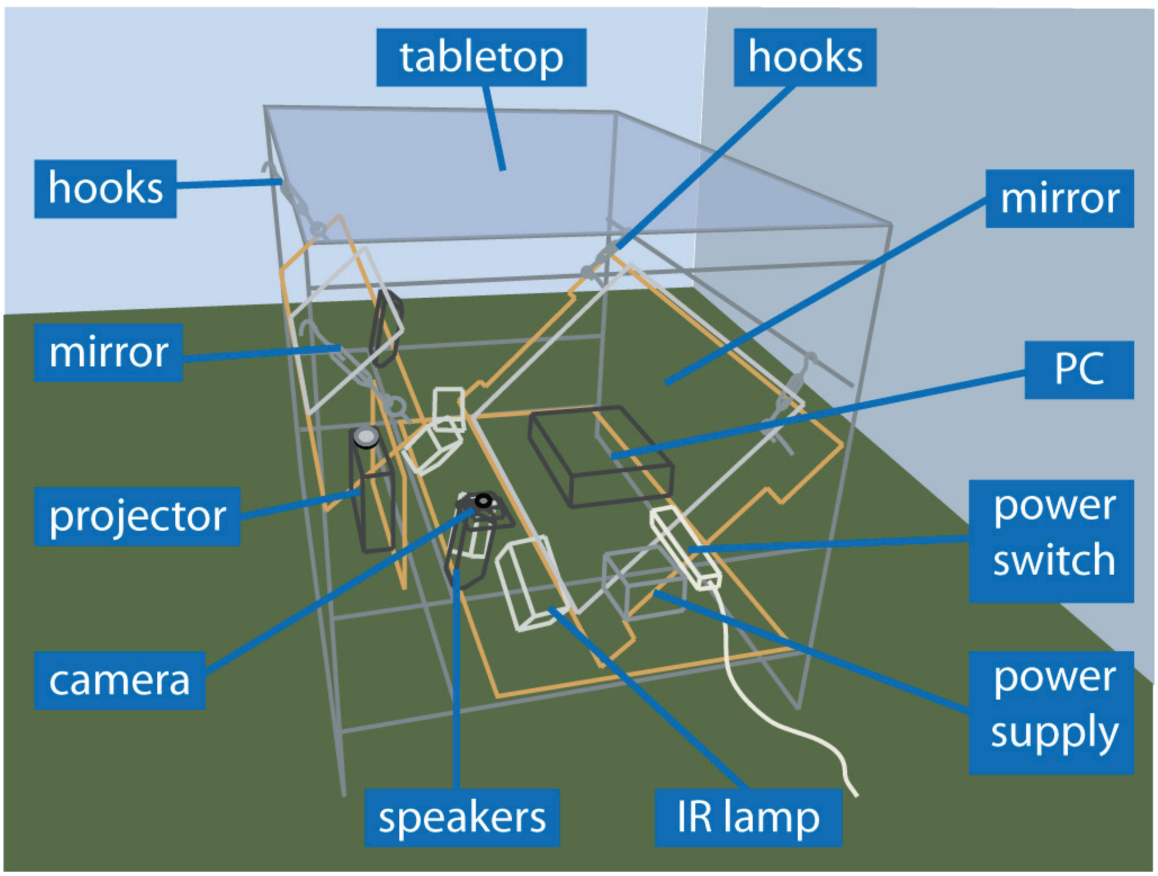


Figure 4-1 The Tangible Tracking Table.

Since the TTT puts more emphasis on tabletop applications than on sensing technology, I adopted reacTIVision [Kaltenbrunner and Bencina 2007] as a bridge to communicate between the physical devices and applications. Consequently, members of our lab concentrated on the development of client side applications, such as multi-user games, educational applications, storytelling applications, collaborative working spaces, geographical navigation, and information visualization. One objective of designing this tabletop interface is to create a large interactive projection surface that allows multiple users to work together at the same time. Therefore, I planned on creating a 60-inch table in the beginning. To create a 60-inch projection screen in a 39-inch tall table, I put two parallel mirrors inside the table. When these two mirrors are placed in the right positions and angles, they can create a 72-inch optical path, which results in a 60-inch projection area (see Figure 4-1). The tabletop is a 36-inch by 48-inch acrylic sheet with tracing paper on top of that, which acts as a diffuser. The detail of constructing this tabletop is described in Appendix – A.

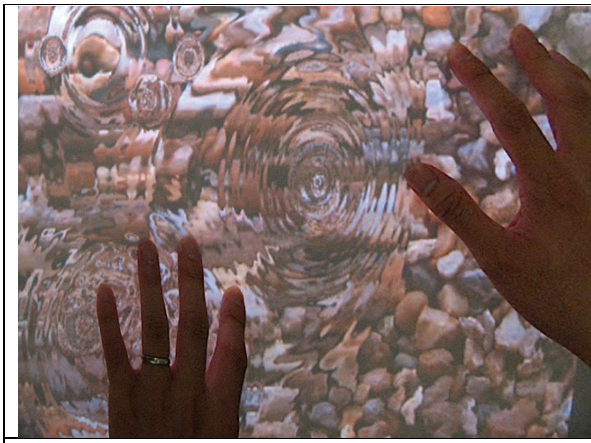
reacTIVision can track multiple finger touches on a surface. It can also track physical objects, which have special designed fiducial markers attached underneath them. reactIVision uses the TUIO protocol, which is based on the Open Sound Control (OSC) protocol, and therefore can easily communicate with other programming environments. In order to detect fiducial markers and fingertips, the table uses a setup of Diffused Illumination (DI) to light up the bottom surface of the acrylic sheet. The concept of DI uses light sources to brighten the inner tabletop surface so that a camera can capture the images of the objects on the tabletop, which is diffused by the light sources. In our setup, the infrared lamps inside the table provide light for the camera to see the patterns of the fiducial markers. An infrared (IR) filter in front of the camera keeps the reflected light from the IR lamps and removes the unwanted visible light. Another visible light filter is placed in front of the projector lens to keep only visible light and remove IR light. The appropriate combination of the IR lamps, the IR filter, and the visible light filter allows the camera to capture the 850nm part of the spectrum, which contains the finger touches and fiducial patterns on the tabletop.

However, it is possible that other 850nm light sources can confuse the system. One limitation of reacTIVision is the number of fiducial markers, which is currently limited to 180. Yet, this is more than sufficient for projects in this research lab. Another limitation is the size of a standard fiducial marker, which has to be at least 3 inches by 3 inches. The size limitation can be smaller if I redesign the fiducial patterns, which, on the other hand, would also reduce the number of usable fiducials.

4.1.2 Applications

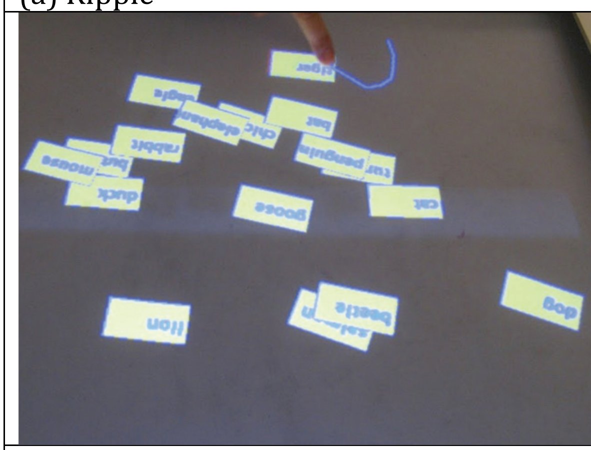
The TTT has given rise to many projects in the Synaesthetic Media Lab (Synlab). The applications include applications for navigation, card sorting, storytelling, games, collaborative sketching, creativity analysis, broadcast studio, mixed reality, and scientific simulations. I played different roles in most of these projects, as a projector leader, a collaborator, or as a supportive lab member.

Some of the earliest applications used figure touches only. The Ripple in Figure 4-2 (a) retrieved finger touch data from the reacTIVision server. After that, the Ripple application simulated water ripples on the table. It was the first application I built for the table. Its only purpose was to demonstrate the capability of an interactive tabletop display on the (Graphics Visualization and Usability) GVU Center demo day. At that time, most visitors had never experienced touching a display and getting immediate visual feedback from the same spot. In another application, a user navigated Google map on the table with her fingers (see Figure 4-2 (b)). She could zoom and pan with finger touches. Also, she was able to jump to a predefined location by placing a bookmarked puck on the map. In 2010, I placed a physical avatar on the tabletop to represent the user. I adopted augmented reality techniques to allow the user to change the zoom level and orientation of the map by lifting and rotating the avatar. Instead of using their fingers, they used the avatar to navigate the virtual world [Wu et al. 2011a].

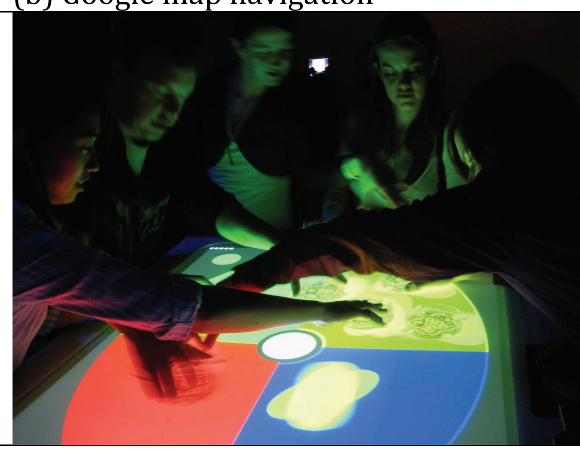


(a) Ripple

(b) Google map navigation



(c) Card sorting



(d) ColorCross

Figure 4-2 Applications developed on the Tangible Tracking Table

The card sorting application in Figure 4-2 (c) was built to show the benefits of performing the card sorting activity on an interactive tabletop. In physical card sorting, it is difficult to trace the activity and record the identities of the cards automatically on a regular table. Usually card sorters use a video camera to record the whole process, but this requires lots of extra effort to transcribe the video. One benefit of this digital card sorting on the table is that all activities are recorded as TUIO messages. Therefore, users can play back all the activities later. Also, compared with software-based card sorting applications, the tabletop card sorting allows multiple users to work collaboratively at the table, which encourages more verbal communication. With the help of this tangible user interface, users can review, analyze and classify items more efficiently than ever.

ColorCross in Figure 4-2 (d) was a four-player game inspired by the game twister [Milton Bradley Company. 1966]. Its goal is to get multiple people physically involved in the game play without having to compete against each other. It is a collaborative game where each player holds two physical objects tagged on the bottom with unique fiducial markers. The table was divided into four color-quadrants: red, blue, green and yellow. As players place their tangibles on the table, color orbs under the objects (which start off white) randomly change to match one of the four colors of the quadrants. The objective of the game is to get every object to match up with the corresponding color quadrant by moving them around the table. At the end of each round of the game, the color orbs switch color again, and players must scramble to rematch the new color orbs with the quadrants. [Synaesthetic Media Lab 2008]

There are several storytelling applications that utilize the advantages of multiple object tracking and multiple touches. This new nonlinear and multi-user experience is different from other digital narrative projects. The two pieces in Figure 4-3 (a) and (b) were designed in an interdisciplinary research and studio class [Mazalek et al. 2009b] across the architecture, industrial design and digital media departments at Georgia Tech in the spring of 2008. The goal of the class was to create an interactive tabletop story experience by combining design and engineering techniques and technologies from architecture (tables and spaces) with digital and tangible media forms (computation, content, and visual arts). Students were challenged to remediate content from the documentary film *Fast, Cheap and Out of Control* [Morris 1997].

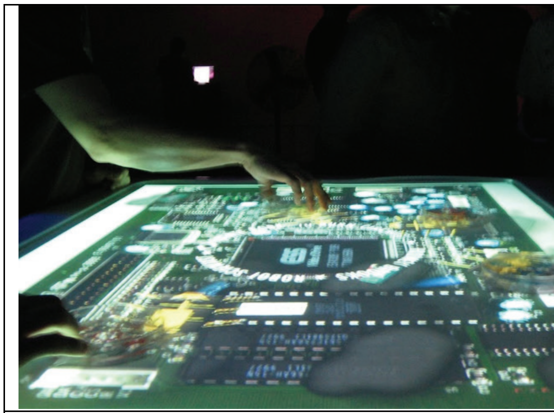
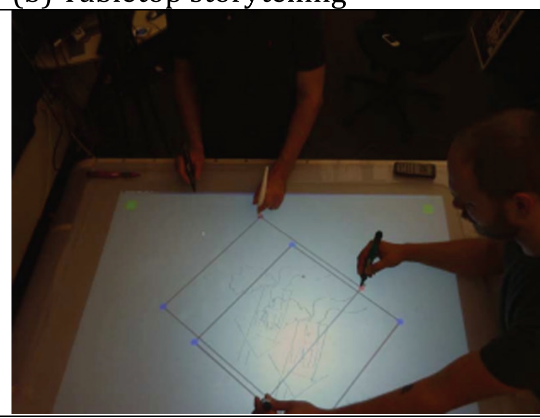
	
(a) Tabletop storytelling	(b) Tabletop storytelling
	
(c) KinoPuzzle	(d) SketchTop

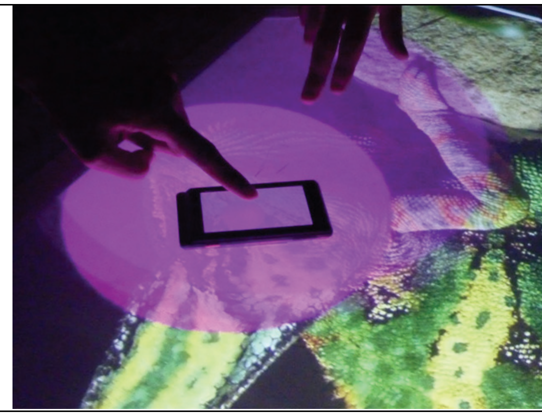
Figure 4-3 Applications developed on the Tangible Tracking Table

KinoPuzzle [Robinson et al. 2009] was a storytelling engine that aimed to create a tool that offers the maximum flexibility for the interpretation and experiencing of mediated realities, including realities in conflict (see Figure 4-3 (c)). My collaborator and I analyzed social and ethnographic documentary works and practices from the social sciences, ethnography and ethnomethodology, to reduce observer bias in documenting and understanding situations from the points-of-view of those involved in situations. One novel concept we introduced to the tabletop was the design of the physics engine API to simulate the attraction and repulsion between the physical objects on top of the tabletop and the digital media projected on the tabletop.

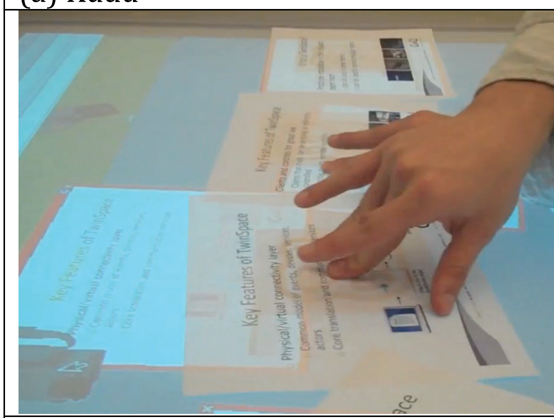
SketchTop [Clifton et al. 2011] in Figure 4-3 (d) was a multi-touch sketching application for collocated design collaboration. SketchTop showed that a tabletop application that supports collocated collaborative design could provide users with the ability to communicate and iterate ideas generated during early phases of the design process. This understanding can lead to further work exploring how digital tabletops can augment the design process by making it more interactive.

The Tangible Tracking Table also furthered creativity research. My colleague and I adopted the Geneplore Model proposed by Finke et al. [Finke et al. 1996] as our implementation framework to discuss the freedom and the constraints within the creativity cognitive process and how an interactive surface can support this creative cognitive process. According to the conclusion of Finke's experiments, a constrained environment may result in more creative production. In other words, too much freedom of creation can limit the creativity of a person. One interesting question is how the freedom and constraints of a medium affect the creativity of people. As a result, we designed Kudu (see Figure 4-4 (a)), an application similar to Finke's experiment, on an interactive tabletop display to explore the creative production between a paper-based interface and an interactive tabletop display. We found that people used different strategies on Kudu. They dragged, rotated, and scaled the shapes to explore the possibilities on the tabletop. Unlike drawing on a piece of paper, these interactions do not map directly to most people's daily activities. Our first version of Kudu did not record the history of the interactions. Therefore, the participants could not see their previous creation when they created a new one. A paper-based interface, on the other hand, always maintains a record of the drawing. Several of our participants admitted that they continuously looked at their previous drawings to gain more ideas.

(a) Kudu



(b) ROSS Ripple



(c) TwinSpace

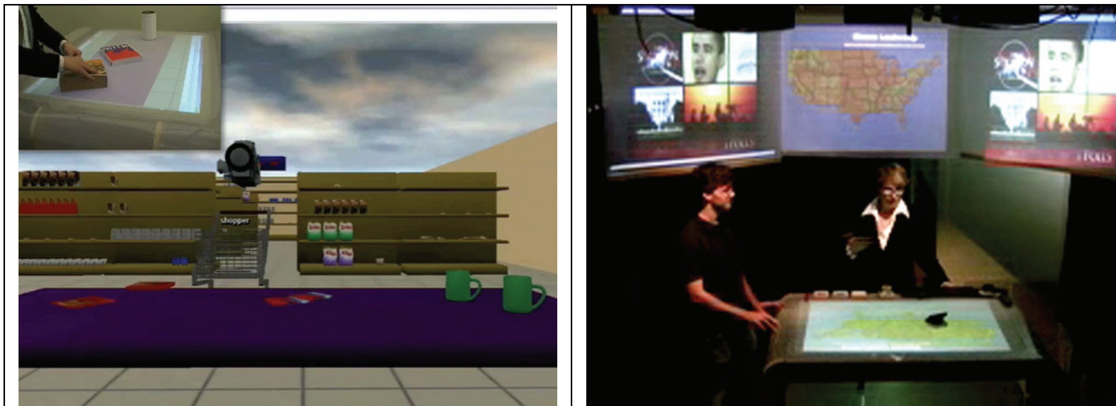
(d) CVE

Figure 4-4 Applications developed on the Tangible Tracking Table

The Tangible Tracking Table is one of many ROSS API projects [Wu et al. 2012]. The capability of rendering graphical visualization and detecting objects on its surface makes the TTT an ideal platform to create visualizations adjacent to multiple objects locations. The ROSS Ripple in Figure 4-4 (b) was an interactive tabletop application that shows the nested structure of ROSS. When the smartphone is away from the tabletop, the image of the smartphone's touch screen is a duplicate of the tabletop's image. When the smartphone is placed on the tabletop, its touch surface has become part of the tabletop. Therefore, a touch signal on the cellphone surface generates a ripple that passes (through) the physical boundary of the phone and progresses to the tabletop, and vice versa.

My ideal tangible embodied interaction is a physical space on/from, which users can obtain information from the physical properties of everyday objects and control the digital world by manipulating these physical objects. An interactive tabletop display provides a platform that allows objects on top of it to easily communicate with the environment (the table) and change the appearance (the tabletop) of the environment. It is an ideal environment to realize some of my ideas before I can find the appropriate interface that can fully support my concepts. TwinSpace [Reilly et al. 2010] is a flexible software infrastructure for combining interactive workspaces and collaborative virtual worlds. Its design is grounded in the need to support deep connectivity and flexible mappings between virtual and real spaces to effectively support collaboration. This is achieved through a robust connectivity layer linking heterogeneous collections of physical and virtual devices and services with a centralized service to manage and control mappings between the physical and virtual spaces. For example, moving the physical paper on the tabletop also moves the virtual document in the virtual environment (see Figure 4-4 (c)). Under the TwinSpace infrastructure, I helped create several experimental tangible interfaces, including a rotary monitor, which allows users to view the tabletop from different angles from a virtual avatar; a trolley that navigates the virtual world; and an interactive tabletop that has multiple functions. I learned and designed several different tangible interactions for navigating a Collaborative Virtual Environment (CVE) on an interactive tabletop display (see Figure 4-4 (d)).

The tabletop interface for navigating CVEs presented a practical application in a conference competition. The goal of this competition was to navigate a supermarket with a shopping cart, pick up items on the shelves, move the cart to a checkout desk, place the items on specific locations on the desk, and rotate them to designated directions. My collaborators and I used the trolley as the shopping cart to navigate the supermarket and the table as the register desk. Figure 4-5 (a) shows that when a user moves a physical pizza box onto the tabletop, the corresponding virtual pizza box also moves in the virtual world. Compared with other CVE controllers, which do not have easy-to-use interaction mechanisms to navigate through the virtual world or to manipulate virtual objects, our method was more intuitive.



(a) Mixed reality supermarket table	(b) Tangible Anchoring

Figure 4-5 Applications developed on the Tangible Tracking Table

Tangible Anchoring [Robinson et al. 2010] is a project that uses smartphones as active objects to demonstrate public opinion visualization on an interactive tabletop display. The application scenario of Tangible Anchoring is an anchor (the user) showing statistical data to the audience watching the broadcast (see Figure 4-5 (b)). The anchor retrieves the data from the active object (the smartphone) and filters the visualization results using passive objects that represent different political groups. The smartphone gives the user a controller alternative to directly using finger touches to enter data on the interactive tabletop display.

After exploring different techniques and interaction designs using tangible objects and interactive tabletops, I started to look at cases where TUIs can be more effective than non-TUIs. Optical Chess, one science simulation game, caught my attention, as it was a newly designed game that was available only with GUI. To demonstrate that TUI improves the way we think and solve problems, I built a tangible version of it, Tangible Optical Chess to show that players of TUI games develop more strategies than players of GUI games.

4.2 Tangible Optical Chess

Optical Chess is a strategy board game that uses the metaphor of lasers and mirrors, the basic optical reflection rule, as well as many of the concepts and terminology from the more standard game of chess. Optical Chess draws from the idea of laser-and-mirror interaction. The game was originally implemented with a conventional GUI interface. The first version of Optical Chess was on a PC. Players could point and click the game window to move the pieces with a mouse by turn. Ideally, this game should be played on a chessboard, like regular chess, with real lasers and mirrors. However, using a real laser for game play presents a potential danger to the eyes, potentially burning the retina of the eye. Moreover, seeing the path of an actual laser is not feasible under normal conditions. An actual laser beam can been seen only when it is scattered by particles, e.g. a wall or dust in the air.

4.2.1 Design

I believe TUI can improve the way people think about and solve problems in game simulations. To support this argument, I created Tangible Optical Chess, a tangible version of the GUI game, Optical Chess, and conducted evaluations to compare these two different interfaces.

The game is played on a square grid of some tiles by two players (Green and Red). Each player has three types of pieces that can be placed upon the board: one

“King” (the target for one's opponent), one laser (the mechanism for attacking the opponent's King), and several mirrors (used for reflecting the lasers around the board). The game begins with each player (Green first) placing their King on any space of the board except spaces bordering the edge. After each player places their King, the players take turns. On a player's turn, they may do one of four things:

- Place, move, or remove their laser.
- Place a mirror at a 45-degree angle to the grid on any unoccupied game space.
- Rotate one of one's own mirrors 90 degrees.
- Remove one of one's own mirrors from the grid.

The objective of the game is to hit the opponent's king with one's own laser, using at least one mirror. Unlike chess, an Optical Chess player must announce “Check” one move before placing a winning move.

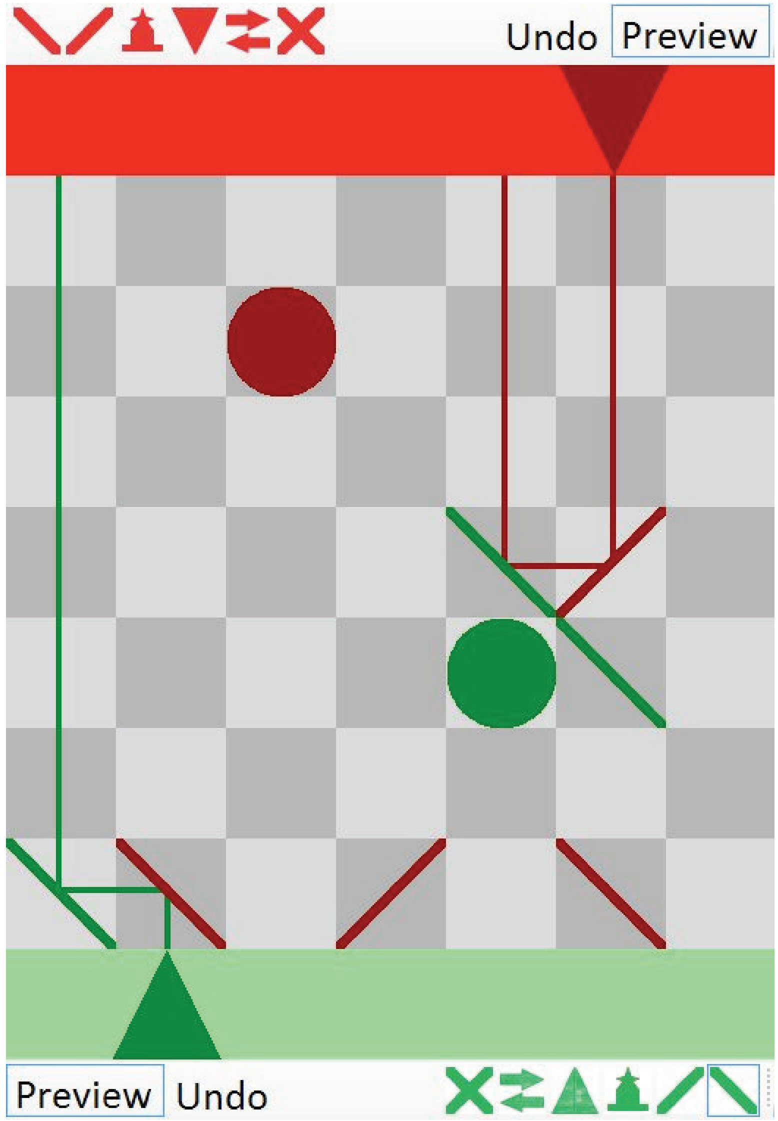


Figure 4-6 The GUI version of Optical Chess.

The initial design of Optical Chess results from careful analysis of existing games. The four goals for the creation of Optical Chess are that it (1) be easy to learn, (2) be very difficult to master; (3) be strictly strategic (no randomness, and thus no dice or cards); and (4) lend itself to complex strategies that emerge from a simple rule set. This analysis led to the fundamental building blocks of the game: namely, that the game would feature lasers, mirrors, and a “king” that would serve as the target for the opponent.

Initially, the game was prototyped with a GUI. Figure 4-6 shows the GUI interface for Optical Chess. The circles represented kings, the slashes (\ and /) represented mirrors in different orientations, and the triangles represented the lasers. Players had to share a mouse to point and click on the icons by turn. One could place a mirror in "\"or "/" orientation, place the king, place and fire the laser, and rotate or remove one mirror by selecting the six icons from the toolbar. The laser beam traveled in a straight line and changed its direction 90 degrees when deflected by a mirror.

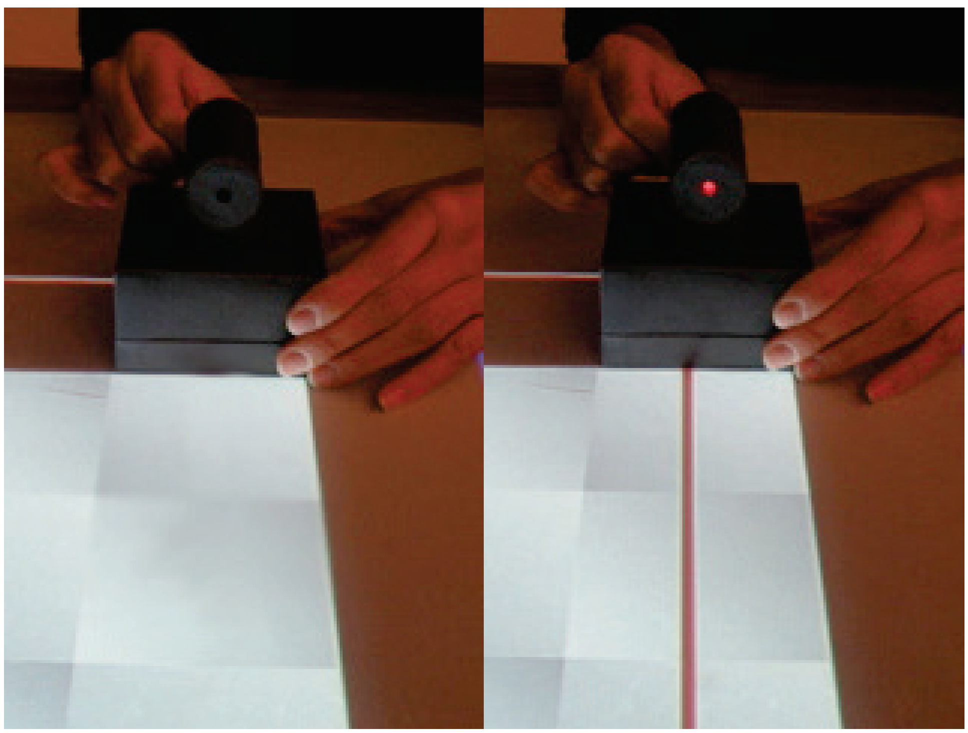


Figure 4-7 The user turns on the laser (right). The table detects the fiducial and shows the laser path. The laser is turned off (left).

As soon as the game's viability was confirmed on the GUI version, a full implementation was designed using the TTT. The chessboard is designed in 7 by 7 squares, each of whose sides are about 4.5 inches. Each chess piece is about 4 inches wide. There are three types of pieces, one king, one laser, and several mirrors, and each affects the simulation differently. According to Bakker et al. [Bakker et al. 2007], these iconic physical pieces are fundamental to a tangible tabletop game since they add a sense of fun. We modeled our game pieces after real-life optical components in a laboratory. Hence the laser piece has a black laser tube sitting on top of a black box (see Figure 4-7) and the mirror has a black round base with a colorful frame to identify its side (see Figure 4-8).

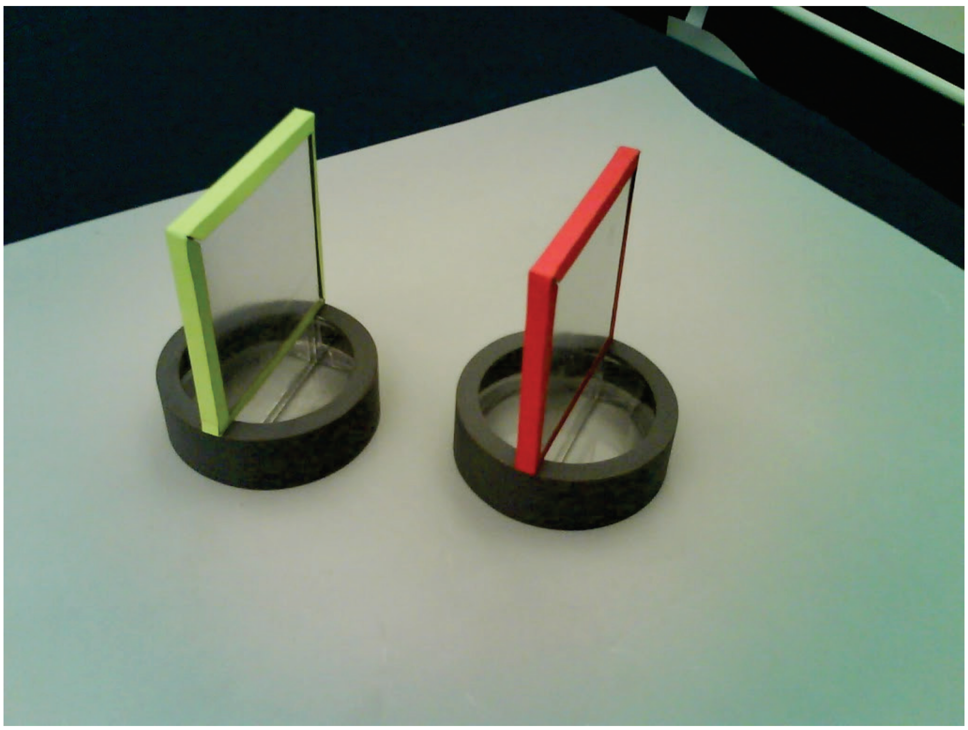


Figure 4-8 The mirrors of the two campaigns.

The laser object has a simple mechanical arm and an electric circuit inside. On top of the black box, right under the tail of the black laser tube, there is a switch. The laser has an adjustable base, which can be elevated. When one switches on the laser, the LED inside the tube turns on and the arm inside the box lowers the base with a fiducial marker to the tabletop. When the laser is switched off, the arm lifts the base, and the fiducial marker leaves the tabletop. In this way, one can turn the laser on and off and see the reactions of the LED and the beam on the tabletop simultaneously (see Figure 4-7).

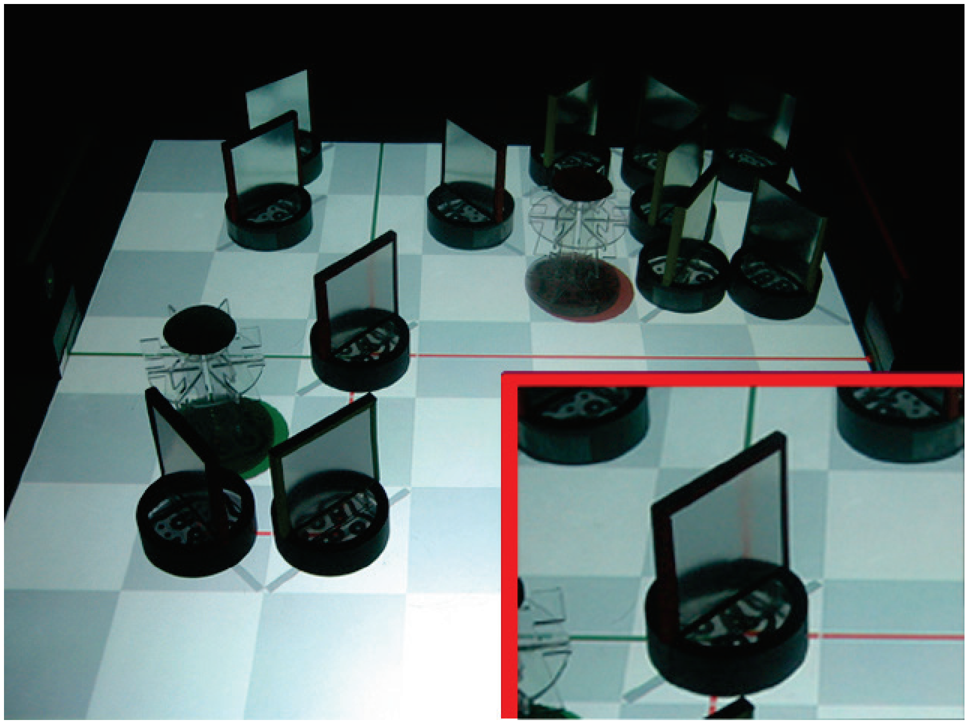


Figure 4-9 The end of one game set and a close look at a mirror.

The “mirror” of the physical mirror object is made of silver reflective paper; all the physical objects are made of acrylic sheets and colored paper. The fiducial markers can be seen clearly since the base of each chess piece is made of a transparent acrylic sheet. A closer look at the red mirror shows the laser beam reflected on the tabletop. Still, the silver reflective paper on the mirror surface reflects the image of the laser beams (see Figure 4-9).

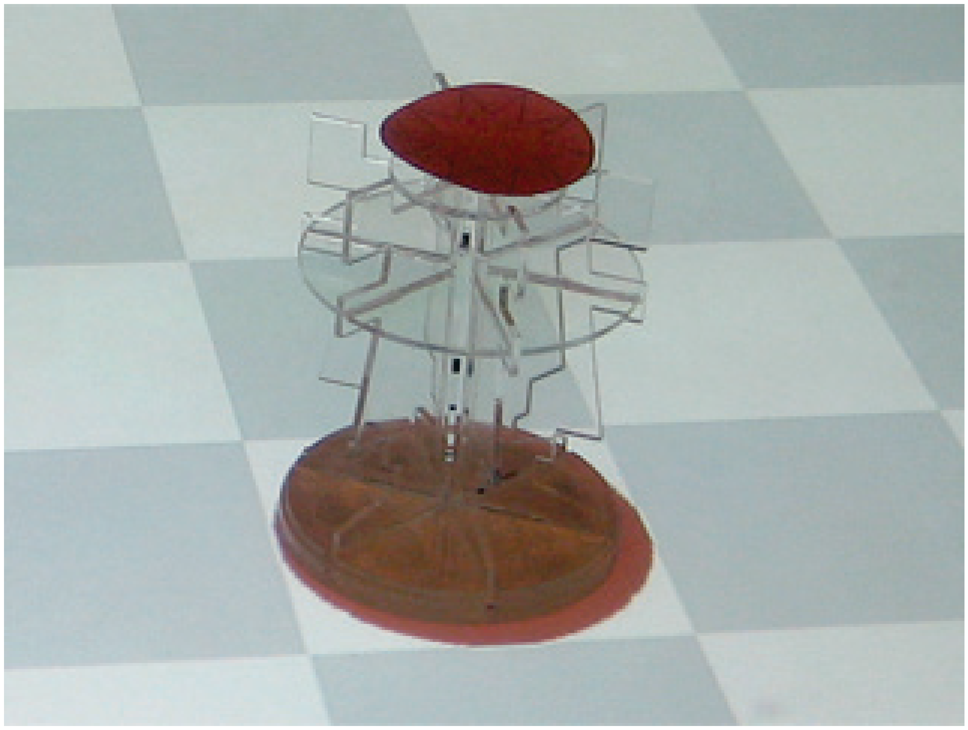


Figure 4-10 The red king, the target of the green opponent

I designed the kings (see Figure 4-10) using the combination of a king's crown and castle battlements. Once the king is placed, the player cannot move it. Laser beams stop propagating when they hit any side of a king.

Optical Chess is a strategy board game that uses the metaphor of lasers and mirrors, a basic optical reflection rule, as well as many of the concepts and the terminology from the more standard game of chess. Optical Chess draws from the idea of laser-and-mirror interaction. The game was originally implemented with a conventional GUI interface. The first version of Optical Chess was on a PC. Players could point and click the game window to move the pieces with a mouse by turn. Ideally, this game should be played on a chessboard, like regular chess, with real lasers and mirrors.

Some type of digital visualization of the laser beam can be used to allow safer gameplay, and the enhancement of multimedia can improve the playfulness of a laser game. An interactive table is an ideal interface on which to build Optical Chess. It is a tabletop interface that can display digital information and track multiple tagged objects on top of it. Furthermore, the graspable physical objects provide tactile feedback, which is similar to holding a chess piece. This is why we created Tangible Optical Chess by combining two discrete systems into one interactive tabletop game. The Tangible Tracking Table provides a medium for demonstrating the otherwise difficult-to-prototype Optical Chess, while the Optical Chess game provides an example application for demonstrating the capabilities of an interactive tabletop display. This implementation allows the game to be played on a table, similar to other board games, while the computing power simulates the game mechanics.

4.2.2 Evaluation

The preliminary observation of players of the GUI Optical Chess suggested that two core features are necessary for designing the tangible version: (1) visual feedback of the laser beams, and (2) physical chess pieces that resemble traditional optical instruments. My collaborator and I integrated the GUI version with the Tangible Tracking Table. Therefore, the virtual Optical Chess pieces could be manipulated through tagged physical objects on the tabletop. After that, I built the *mirrors,* which are similar to mirrors used in an optics laboratory and the *lasers*, which look like miniature lasers.

My collaborator and I demonstrated the GUI and tangible version of the game to several different groups of students and observed their interaction with both the game and the table. We also showed Tangible Optical Chess to visitors on our research center's demo showcases. We gained more general feedback from the players and the audience in these occasions. During these demonstrations, players learned from a printed set of rules; researchers were on hand to answer questions and clarify the rules as well as explain the workings of the Tangible Tracking Table. We focused on the types of questions players asked (or the challenges that were observed that would be clarified by questions), the types of strategies players developed, identified through observations of their play style and what was said during play, and how easily the players interacted with the tangible game.

The evaluation results suggest that players of Tangible Optical Chess spent more time organizing the game strategies than players of GUI Optical Chess. I noticed on several occasions that players tended to learn the rules of the game much faster when using the tangible version of the game. The result shows that Tangible Optical Chess seemed to facilitate faster learning likely because players are able to experiment more naturally with tangible game pieces. GUI players did not develop multiple-move strategies, but tangible players did. We observed that players at the TTT spent a much longer time planning their next moves. GUI players tended to only look at the current board, while tangible players would plan subsequent, later moves. We verified this in our demo showcases by asking players what they were thinking while they paused during the game. The tangible players also tested their moves often, especially when they first approached the table. Furthermore, the tangible pieces were attractive to people. The physical mirrors and lasers seemed to really help players to merge with the game. Because the silver paper on a mirror reflects some of the image close to the mirror, many players became confused after they played for a while: they thought the mirrors actually reflected the laser beams.

The Tangible Tracking Table was a very engaging platform for implementing the Optical Chess game. Players engaging in the game associated the strategy in Optical

Chess with other games. Even though the TTT appeared to be an ideal platform for this game, we did not fully exploit its capability. The study results between the GUI and tangible versions showed us that tangibility is a factor that improves playability in Optical Chess.

What I learned from Optical Chess is that changing the presentation changes the way people think about a problem. Even though there was no formal evaluation to measure the exact amount of time players spent on the TUI version versus the GUI version, the observations and interviews strongly suggested that players thought more steps ahead and developed more complicated strategies on the tangible platform. This discovery and the success of Foldit inspired me – I might be able to create a tangible representation of an abstract problem or model and show the effectiveness of being tangible.

5 Kinesthetic Pathways

To demonstrate that tangible interaction can provide a means for researchers to think through the connection between motor, perceptual, and cognitive processes, my collaborator and I designed and developed Pathways, a tangible visualization application designed to realize kinesthetic interaction on an interactive tabletop. Kinesthetic Pathways is designed solve complicated computational modeling to support scientific discoveries. As I mentioned in the first chapter, Foldit inspired a part of the Pathways idea. A central component of the success of Foldit is its direct manipulation interface, which allows players to grasp and pull and move and twist different protein strands. This type of interface, in which the user actively controls and explores objects on screen to develop an understanding, is common in educational applications in science (e.g. PhET [Perkins et al. 2010]). However, most scientific visualizations do not seek to support this type of kinesthetic interaction-based discovery [Davis 2002]. Rather, they seek to represent data in new ways, and the insight is expected to come from the different visual perspectives on the data.

I want to extend such kinesthetic interaction for discovery to systems biology, particularly to the modeling and simulation of metabolic systems, which is a more complex and abstract problem than protein-folding, as the entities involved do not have spatial features and the number of variables are unknown. The exploratory research results of Tangible Optical Chess suggested that tangibility promoted the strategies of players during the game. Moreover, the experience of designing tangible interaction on an interactive tabletop allowed me to quickly create tangible tabletop applications, and I would like to realize this new interface on an interactive tabletop. In the following section, I will describe the problem space of modeling in biological systems. After that, I will present the iterative design of Pathways, the tangible interactions of it and the visualizations in Pathways.

5.1 Practices in a Systems Biology Lab

In this section, I provide an outline of the practices and problems in a systems biology lab, based on a two-year ethnographic study done by my collaborators [Chandrasekharan and Nersessian 2011]. In their research, they studied problem-solving practices in two integrative systems biology labs. I focus here on one lab that does only computational modeling ("Lab G"). The modelers in Lab G are mainly from engineering fields, but they work on building computational models of biochemical pathways to simulate and understand phenomena as varied as Parkinson's disease, plant systems for bio-fuels, and atherosclerosis. The problems Lab G modelers work on are provided by outside experimental collaborators, who see modeling primarily as a method for identifying key experiments of scientific or commercial importance. The collaborators provide experimental data for modeling. The modelers usually separate this data into two parts, one part for developing pathway diagrams (training data) and the other for validating the model (test data). The modeling process can be classified into three phases – building, fitting/testing, and perturbation – even though these phases overlap. In general, the process is built up with small models in the beginning, each going through these three phases. More elements are then added to these models, and these complex models then go through the three phases. The process was described in detail in our previous work [Wu et al. 2011b].

The modeling process through the perspective of data flow from a modeler's point of view is shown in Figure 5-1. The first step in this building process is to get the experimental data from an experimental lab. Usually the data is just a few scattered points sampled from a whole experimental data set. After that, the modeler drafts a model over a wide set of papers based on the previous modeling experience, the information provided from the experimental collaborators, and literature review. However, the modelers, who mostly come from engineering backgrounds, have to estimate the details of the pathway by themselves, particularly the values of parameters related to metabolites, such as the speed of change (kinetic order) and the concentration level (rate constant), which are usually not measured by experimenters. A set of corresponding math models, in this case, usually in the form of Ordinary Differential Equations (ODEs), is also converted from the draft of the model. The next step is to program the math model in a programming language such as MATLAB. Once the program is written, it needs initial conditions to start the simulation, which generates the simulation result. The simulation results are then compared to the actual experimental data to judge the 'fit' of the model. If the two data sets do not fit, the modeler has to either reconfigure new initial conditions or create a new model. This is an iterative process until he finds a solution. If the two data fit, the modeler has found a candidate solution, which will be sent to the experimental lab for another examination to verify. If the data passes this examination in the experimental lab, the modeler might have found the solution; otherwise, he has to go back to either reconfigure the initial condition or recreate the model. The objective of Kinesthetic Pathways is to create a tabletop modeling process that covers the blue part in Figure 5-1. There have been many efforts to visualize the model or create the model. However, not much research addresses the fitting process. This thesis focuses on developing a tangible tabletop fitting experience (the red surrounded part in Figure 5-1) to help systems biologists improve the efficiency of fitting.

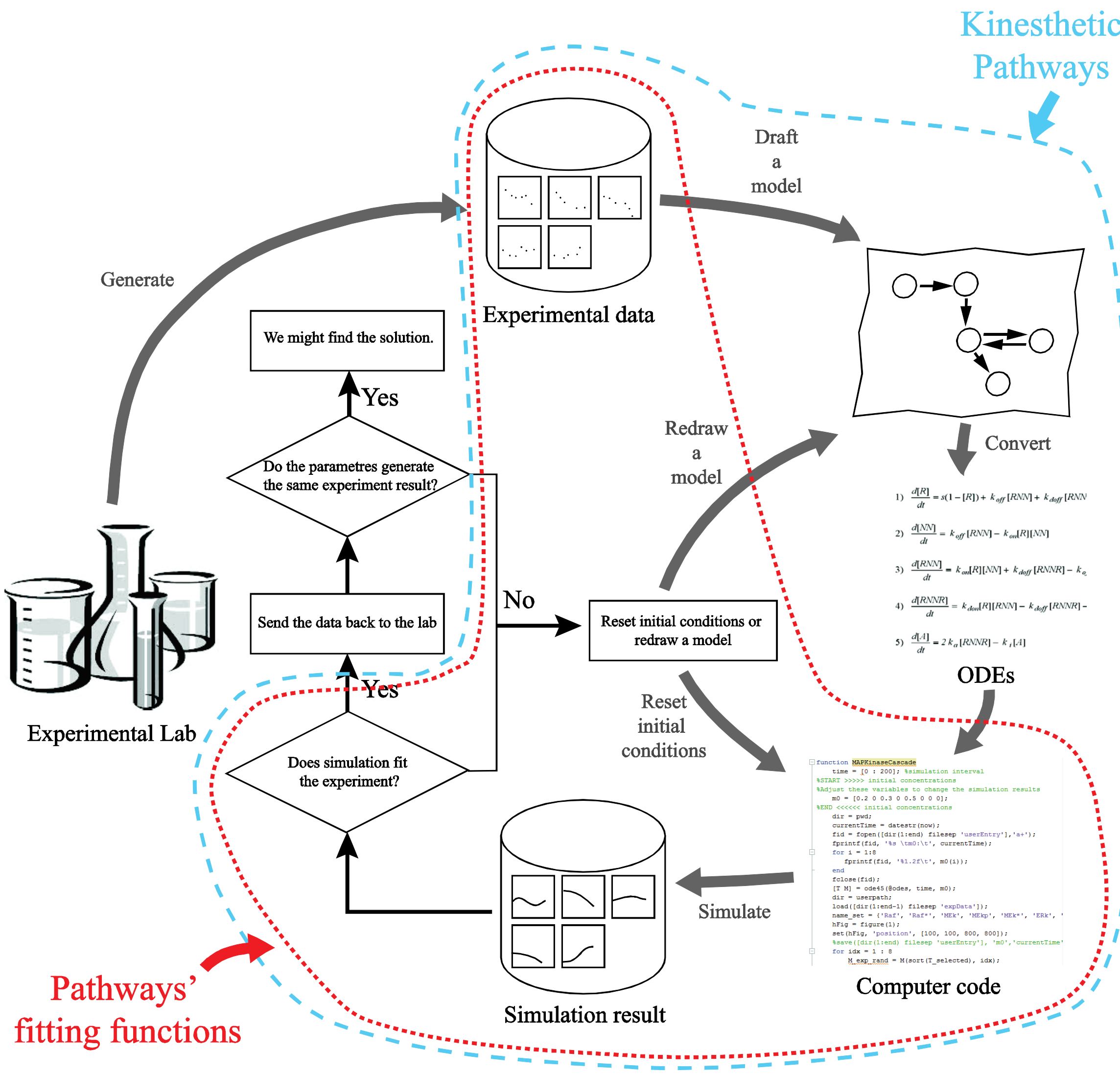


Figure 5-1 The modeling process from the perspective of data flow. The blue dash line is the scope of Kinesthetic Pathways. The red dash line is the scope of Pathways in this thesis.

Modelers from Lab G do not use real-time dynamic visualizations. Parameter values are changed manually or using scripts. Results for different parameter values are compared using a deck of graphs, and each graph plots the concentration value of an element in the pathway across time. The modeler uses these graphs while discussing the model with collaborators and other team members. A significant chunk of the parameter estimation problem is tackled using optimization algorithms (such as simulated annealing and genetic algorithms), which automatically do the 'tuning' of parameters, by comparing the output values (for different parameter inputs) against a desired value. Importantly, the linear workflow suggested by the above description is very deceptive – the modeling process is highly iterative. Usually systems biologists calculate the Root Mean Square errors to estimate how good a set of parameters is.

One of the central problems the lab members face is the unavailability of rich, dependable data. In modeling, data are used for many purposes. One central use of data is to establish that the model captures a possible biological mechanism, and this is done by showing that the model's output matches the output from experiments (fitting data). A second use of data is to tune parameter values during the training phase of building the model. The fit with the experimental data from each training simulation can indicate how the model parameters need to be changed in order to generate model data that fit the training data. This use is highly dependent on the type of data available. Most of the time, the available data are 'qualitative' in nature – usually indicating how an experimental manipulation led to a change in a metabolite level from a baseline. Mostly, this is reported as a single data point, indicating the level going up or down and then holding steady. However, when this type of "steady-state" data fits the results of the model, this fit does not indicate that the model has captured the biological mechanism. A range of parameter values can generate model results that fit such sparse data. In other words, there can be multiple fits. Further, since the pathway is an approximation, the modeler is nearly always uncertain as to whether the lack of a unique and accurate solution is due to a poor estimation of parameters or simply because some elements are missing from the pathway.

5.2 User Scenario

When a user comes to Pathways, she can either load a pre-defined metabolic network into the simulation environment or start from a blank slate. The user creates the elements of the metabolic pathway using both physical and graphical widgets. By stamping the molecule phidget onto the tabletop, she creates a molecule. Following the stamping, a virtual keyboard appears and prompts the user for the name and initial concentration of the molecule. After creating several molecules, she uses either her finger or a stylus to draw lines between molecules, thus creating a reaction network. Now that the network is constructed, she can run the simulation. To start a simulation, she simply places the simulation phidget onto the surface. She can also use a dial phidget to change the values of different parameters.

5.3 The Iterative Design of Pathways

Based on this detailed understanding of the scientific practice in Lab G, I have been developing a tangible tabletop visualization system to support discovery in systems biology with a focus on developing an interface that will allow the researchers to explore parameters in a kinesthetic fashion, and thus estimate the parameters that would best fit model data with experimental data. The system also seeks to support not only modeling by experimenters, who may not have a detailed understanding of the mathematical techniques, but also efficient collaboration between modelers and biologists.

Pathways is a tangible visualization for systems biology. It works with an interactive tabletop display. The interface shows a real-time visualization of the pathway as the simulation is running. Manipulating physical objects on the table changes the concentration and kinetic order values in the simulation. Additionally, the interface provides not only a display of the graphs associated with the pathway, but also the possibility of creating the pathway and its associated equations by just drawing pictures on the table, or using objects to create nodes and arrows. The interface allows even a novice researcher to create a network and simulation from scratch and see both the global changes (the entire network) and the local changes (the graphs) when she manipulates parameter values kinesthetically. In the following sections, we outline some related work, and describe the current prototype, then present the feedback from users, and how we are planning to revise the prototype based on this feedback.

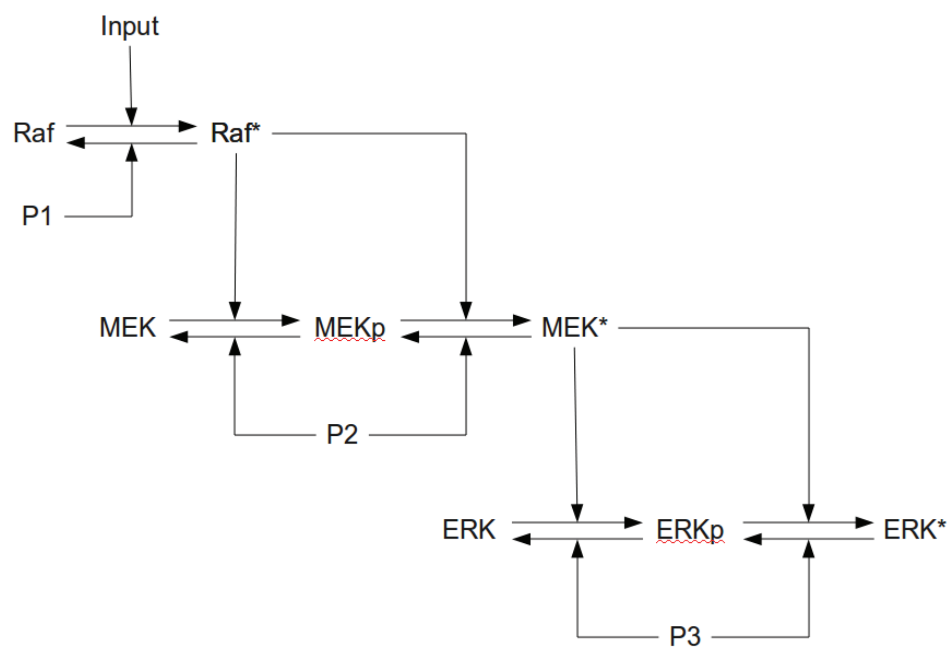


Figure 5-2 A draft of the MAP Kinase cascade. ***Raf*****,** ***Raf***,** ***MEK*****,** ***MEKp, MEK*, ERK, ERKp*****, and** ***ERK**** **are molecules.** ***Input, P1, P2,*** **and** ***P3*** **are enzymes.**

We interviewed our systems biologist collaborators to understand how they (typically) sketch a graphical pathway and to see what other pathways look like. We found that no standard method for drawing a pathway. One common characteristic of most pathways is the use of directed graphs. The nodes of these types of graphs are usually enzymes or molecules, and the directional edges specify the reactions. The default data running on our current implementation of Pathways is the MAP Kinase cascade in the MAPK/ERK pathway. There are 8 molecules and 4 enzymes in this pathway. A draft of the pathway from one systems biologist is shown in Figure 5-2.

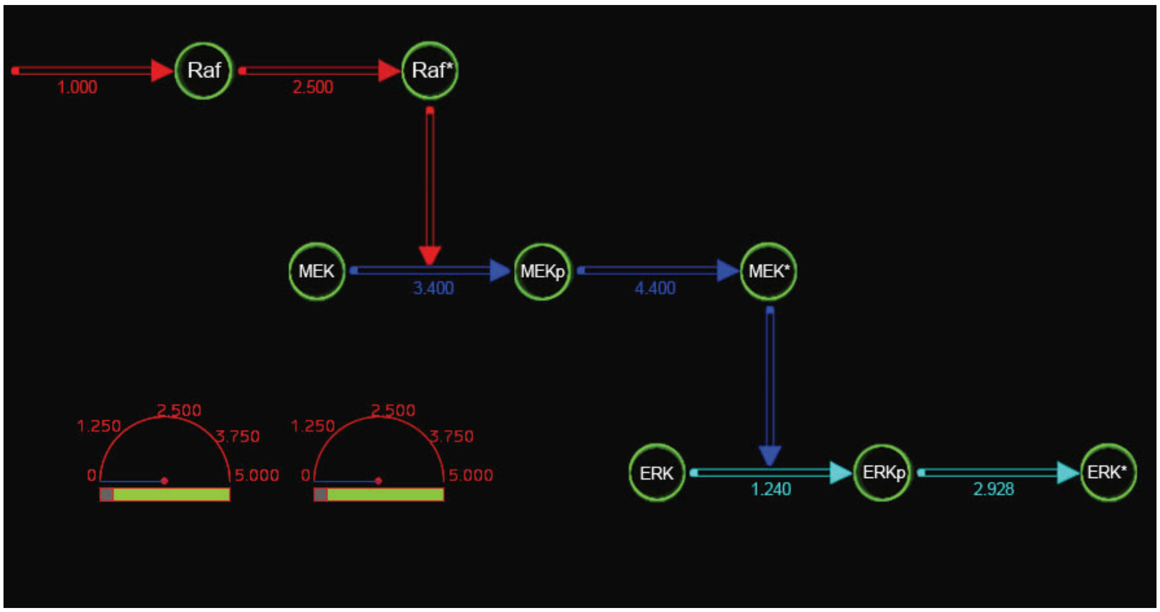


Figure 5-3 The first Pathways prototype developed using Processing

The design process was iterative. My colleague and I had developed at least four major versions of prototypes and several minor versions. My colleague first created a GUI prototype of one simple reaction using Processing (see Figure 5-3) and asked for feedback from a systems biologist. The goal was to gain feedback regarding the two digital controllers at the bottom left of the figure. In order to change the values, one had to use the mouse cursor to slide the green bar under the controller. On each reaction, there was a dot animation moving toward the next molecule to show that the reaction was happening. The interaction was not intuitive, and the prototype did not simulate the model it presented, but we learned a few things from the user:

- The user expected to be able to manipulate the numbers with the mouse directly.
- The visualization or animation should reflect the real data. For example, a thicker line means a faster reaction and a larger molecule circle represents a higher concentration value.
- Systems biologists need graphical output charts to understand the data.
- If the application cannot run a simulation, it is useless for modeling.
- The visualization provided should be more informative. Important information such as concentration values and reaction constants was missing.

Based on the systems biologist's feedback, I created a second prototype using Processing (see Figure 5-4). This prototype was an interactive tabletop prototype. The model in this prototype was more accurate than the previous one. The yellow circles represent enzymes and the yellow arrows symbolize catalyzing reactions. The molecules were in green circles. The red arrows were regular reactions. These biomedical elements used animations to emphasize their states. For example, the speed of a shifting arrow reflected the speed of the reaction, and the vibration of a molecule indicated its current concentration. This prototype started a real simulation when the program started. A was also a timer that started counting with the simulation. In addition to the new visualizations, I added two tangible controllers, the dial and the output chart puck. The dial was used to select a molecule and change the initial concentration of that molecule. Placing the output chart puck on the tabletop plotted the concentration changes of all the molecules.

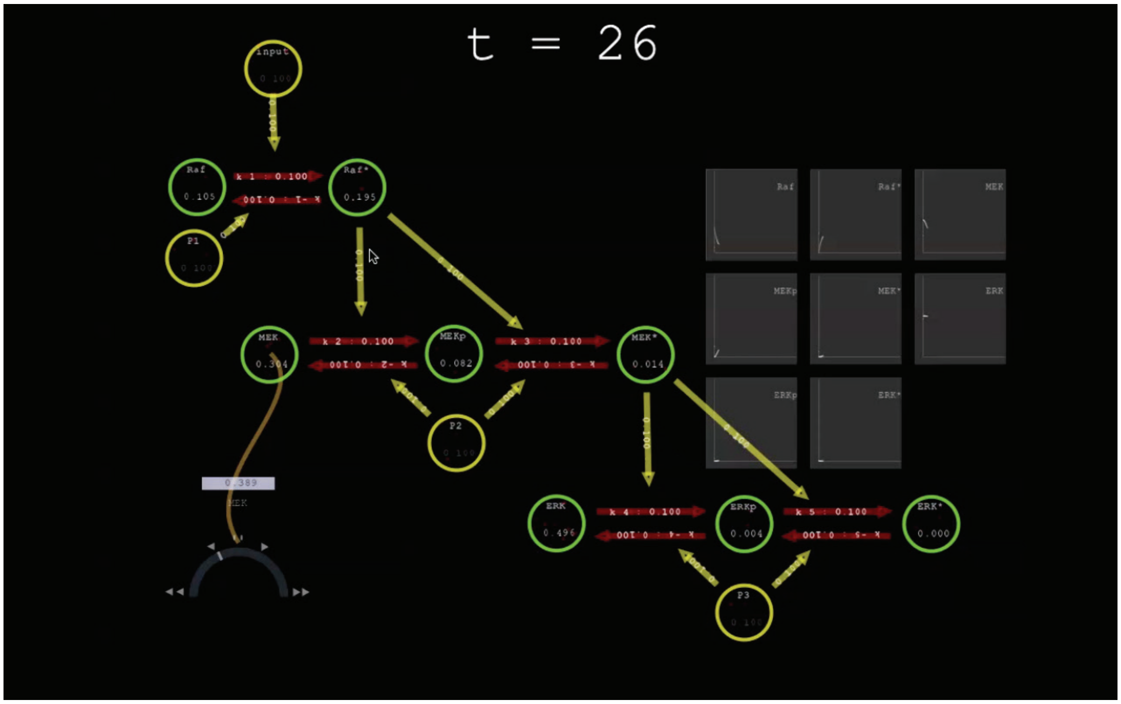


Figure 5-4 The second Pathways prototype developed using Processing

We invited three systems biologists again to look at this prototype. They showed a positive attitude toward the progress and gave us some feedback:

- Only the initial concentrations of 8 molecules were adjustable. The users wanted to adjust the reaction constants, too.
- The vibration animation of the molecule was distracting. Perhaps changing the size of the molecule would be easier to understand the concentration changes of the molecule.
- The output chart plotted slowly as the time progressed. The users had to wait for a long time to see the output results, which did not help modeling.
- The idea of the dial was interesting. The users felt that this function would be more valuable if it could have changed the concentration value of the selected molecule.

- The users wanted to see the ODEs of the model.
- One systems biologist wanted to restructure the model in a way that mapped to her mental model. For example, moving *Raf* and *Raf** to the top right corner of the display.

At this point, we had confirmed that to make Pathways a useful tool, real-time simulation was necessary. Therefore, I started to write a Java-based Pathways program using some Java libraries, such as Processing [Fry and Reas 2011] and Multi-Touch for Java (MT4j) [Laufs et al. 2010]. MT4j is a library design for multi-touch Java programming. Its purpose is to support different kinds of input devices but with a special focus on multi-touch support. It uses a hardware abstraction layer to support a number of different hardware input devices. It allows anyone to add functionality to support a new device by extending the abstract super class of all the input sources. MT4j contains a number of presentation layer affordances, such as scenes to separate various parts of applications, extensible components, and a canvas and rendering layer. Additionally, these GUI components support event propagation, listening and processing to handle the input events from the hardware components. MT4j predefines several multi-touch gestural interactions, and the architecture is sound and robust. It also supports the TUIO protocol, which could be easily integrated into the TTT. I recreated visualizations similar to those in the previous version of Pathways, but gave them a more organic appearance (see Figure 5-5). The dial was able to change the initial concentration of a molecule and restart the simulation. The simulation finished in less than 100 milli-seconds, and the output charts were plotted immediately. To highlight the current time in each output chart, I added a vertical red line that moved along the x-axis as the time progressed. The output charts were also draggable by finger touches. This prototype was very close to the current version of Pathways. My collaborators and I asked the systems biologist to use this system, and we received valuable feedback about the fitting process from him.

Basically, he thought this version was closer to a useful tool than the previous versions but that it required some special functions:

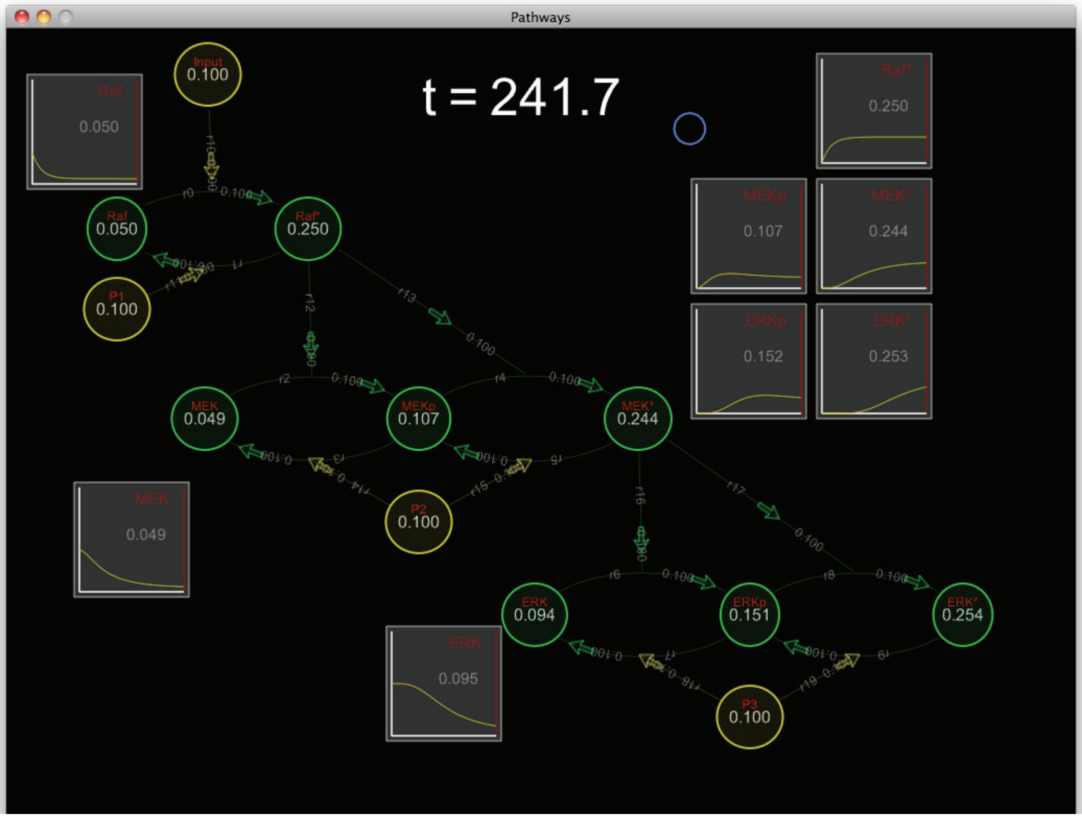


Figure 5-5 The third Pathways prototype

- Systems biologists tune not only the initial concentrations of the molecules but also the reaction constants.
- Without comparison between the simulation result and the experimental data, this application was still more useful for demonstrations or educational purposes than using for real tasks.
- At this stage of the project it was expected that Pathways would have save/load/edit functions.

- Pathways should have been able to perform comparisons to see the differences between two initial conditions.
- Making the output charts movable was a good idea, but there should be a function to gather them to one location.
- The zoom function is helpful, but instead of standard zooming that only magnifies information in more detail, it would be more valuable to be able to see semantic zooming, which reveals semantically relevant information while zooming to different levels.

A fourth prototype has been redesigned exclusively for user evaluation. I will talk more about this prototype in the evaluation section.

5.4 The ODE Model

The underlying math of a pathway is a series of Ordinary Differential Equations (ODEs) that represent the producers and consumers in the chain reactions. There are several other different math models that can simulate a biomedical pathway. Among them, the ODE model is probably the simplest one. Currently, systems biologists have to write programs to solve these ODEs. Once Pathways is completed, we expect them to interact (directly) with the graphical representation of the data. There are several mathematical libraries available for solving the ODE set. We tried two different approaches to create a sample pathway.

5.4.1 Graphical Pathways with Supporting Math

The idea of using graphics to representing math is to allow the systems biologist to create a pathway on an interactive tabletop display. This can be done using either a graph description language or the tools provided by our tabletop application. DOT, a language designed to describe graphs, is used in the current prototype. Because DOT is good for describing complex graphs, I used this process to simplify the visualization tasks and focused more on the simulation and fitting process. To describe a graph, one has to use the syntax in Equation 5-1.

```
A -> B
```

Equation 5-1

Table 5-1 A DOT file that describes A->B

```
digraph simple_model {
     rankdir = LR;
     node [shape = circle]; A B;
     A -> B [ label = "k1"];
}
```

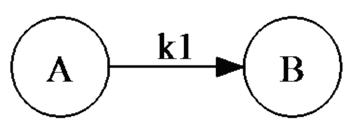


Figure 5-6 The visualization of Table 5-1

This statement describes the start-node A, a directional edge from A to B, and the end-node B. DOT is written in plain text and can be easily parsed by computer programs. The corresponding DOT file content for Equation 5-1 is shown in Table 5-1. The output result using Graphviz, a DOT visualization program, is shown in Figure 5-6. However, one cannot describe a graph using this DOT without actually having a draft beforehand. Assuming the reaction constant of the graph is k and t represents time, the ODEs of that graph can be written as:

$$\frac{dA}{dt} = -k \cdot A$$

Equation 5-2

$$\frac{dB}{dt} = k \cdot A$$

Equation 5-3

The "-" sign in Equation 5-2 shows that the concentration of A is decreasing as time progresses. The law of conservation of mass states that the mass of an isolated system will remain constant over time. Therefore, combining the two equations above gives us:

$$\frac{dA}{dt} + \frac{dB}{dt} = 0$$

Equation 5-4

Equation 5-4 looks like a trivial equation. However, an experienced systems biologist can apply this equation appropriately and find better fitting solutions. Using Equation 5-2 to Equation 5-4, I created a set of ODEs that describe Figure 5-2. Since there are eight molecules, there are 8 ODEs. The ODEs are shown in Equation 5-5.

$$\frac{dRaf}{dt} = -k_1 \cdot I \cdot Raf + k_2 \cdot p_1 \cdot Raf^*$$

$$\frac{dRaf^*}{dt} = k_1 \cdot I \cdot Raf - k_2 \cdot p_1 \cdot Raf^*$$

$$\frac{dMEk}{dt} = -k_3 \cdot MEk \cdot Raf^* + k_4 \cdot p_2 \cdot MEKp$$

$$\frac{dMEKp}{dt} = k_3 \cdot MEk \cdot Raf^* - k_4 \cdot p_2 \cdot MEKp - k_5 \cdot Raf^* \cdot MEKp - k_6 \cdot p_2 \cdot MEk^*$$

$$\frac{dMEk^*}{dt} = k_5 \cdot Raf^* \cdot MEkp - k_6 \cdot p_2 \cdot MEk^*$$

$$\frac{dERK}{dt} = -k_7 \cdot MEk^* \cdot ERK + k_8 \cdot p_3 \cdot ERKp$$

$$\frac{dERKp}{dt} = k_7 \cdot MEk^* \cdot ERK - k_8 \cdot p_3 \cdot MEKp - k_9 \cdot ERKp \cdot MEk^* + k_{10} \cdot p_3 \cdot ERk^*$$

$$\frac{dERk^*}{dt} = k_9 \cdot MEk^* \cdot ERKp - k_{10} \cdot p_3 \cdot ERk^*$$

Equation 5-5 The 8 ODEs that describe the model in Figure 5-2

5.4.2 Math with Graphics

Another approach is to allow the user to enter the ODEs or the Systems Biology Markup Language (SBML) [Bornstein et al. 2008; Szallasi et al. 2006]. After that, the system generates the pathways based on the equations. Eventually, the biologists have to approach the tabletop to interact with the visualizations on the tabletop surface. In this approach, the user can concentrate on the numerical data and mathematical equations rather than on the visual representation of the data. However, few people can think with ODEs only, especially when the pathway grows larger. Even if some claim they do, they most likely have graphical representations of data in their minds. As a result, even though the graphical presentation in Pathways was created from ODEs, I hid the equations and showed the graphics only.

I could also imagine a possible third option, which is to first create the model with one of the two methods mentioned in the previous sections, and then use the other method for further editing.

5.5 Simulation

In the proposed Pathways system, a user drafts molecules by using the visual tools provided by the tabletop. After that, she creates reactions between molecules by dragging her finger from one molecule to another. The ODEs are generated when she creates the pathways. This approach is intuitive, but the user needs to have a rough pathway image on her mind in advance to create the graph. Another drawback of this approach is that the freedom of creation can create unreasonable chemical chain reactions and unsolvable pathways. This problem is partially offset by the knowledge of our users, who are very familiar with their domain.

To create a new model in the current Pathways, one first has to create the graph of the model using the DOT language and generate the output file in the Scalable Vector Graphics (SVG) format as described in Table 5-1 and Figure 5-6. Pathways then creates the semantic structure of the model by parsing the SVG file. At this point, it has a very good idea of what the model looks like. After that, it generates the ODEs based on the rules mentioned in Equation 5-2 to Equation 5-4. To start the simulation, the ODEs need initial conditions. An ODE group like Equation 5-5 requires the initial concentrations of 8 molecules (*Raf, Raf*, MEK, MEKp, MEK*, ERK, ERKp, ERK**), the concentrations of 4 enzymes (I, P_1, P_2, P_3), and the reaction constants of 10 reactions (K_1 to K_{10}). The ODE solver library calculates the simulation results. In the example of Equation 5-5, it takes less than 100 milli-seconds to simulate the results from $T = 0$ to $T = 200$ ($\Delta T = 1$) on a

Mac mini with a 2.3 GHz dual-core processor. The simulation restarts whenever the user lifts the tangible dial from the tabletop.

Pathways uses MT4j as the multi-touch interaction framework. MT4j provides abundant touch gestures and event handling functions. The visualization of the model is a separated thread. The screen is redrawn when the timer ticks, which is dependent on the user's setting.

5.6 Tabletop Interactions

For the user, it can be hard to decide when to use tangibles and when to use more direct manipulation with finger touches. As the interaction surface supports both the tracking of tangible objects and finger touches, we frequently encountered moments when we needed to choose one method of interaction over the other. With tangibles, only the person holding the tangible has control of the tangible's corresponding digital component, whereas finger touches allow all users an equal chance to manipulate the media on the tabletop. Tangibles thereby lead to scenarios with more centralized control of the simulation and (perhaps) fewer accidental modifications.

There are benefits and drawbacks of using objects for tabletop interaction. One benefit of using tangible objects instead of using finger touches is tangible objects provides robust orientation information on the tabletop. The orientation of the tangible object can be easily mapped to numerical data. As a result, rotating tangible objects to adjust numbers seems to a reasonable choice on the tangible tracking table. A limitation to the current set of tangibles is that they occasionally block the view of the digital content on the tabletop. Since the orientation of a tangible can be determined, the orientation of digital content can be adjusted to face the user. The current build of the application uses tangibles for all major interactions, which include modifying molecule concentrations, adding molecules to the network, positioning the graphs of the ODE, and starting and stopping the reaction simulation.

Figure 5-7 The Sony SLV-E25 VHS video recorder dial controller

One tangible we use is modeled after the dials on old VCR dial controllers in Figure 5-7. When a user rotates the VCR dial clockwise, video speeds up forward. The more she rotates it, the greater the speed. When the user releases the dial, it returns to the balanced state and plays the video at a normal speed. Likewise, a counter-clockwise rotation rewinds the video. The dial in Pathways operates similarly (see Figure 5-8). The dial has two rubber bands in it to provide force feedback. Only instead of manipulating time, it adjusts the initial concentration of a molecule or the reaction constant of a reaction (see Figure 5-9). When a user releases the dial in Pathways, the dial returns to its balance state, and the corresponding number stops changing.

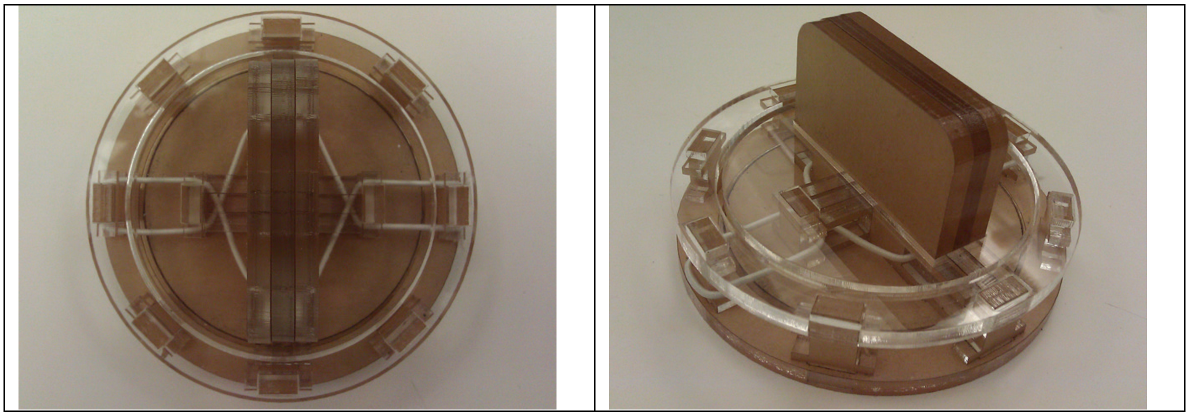


Figure 5-8 The tangible prototype of a dial. This dial is made of transparent acrylic. It is not colored yet. The white wire inside the dial is a rubber band that provides the torque for the dial to "return to balance".

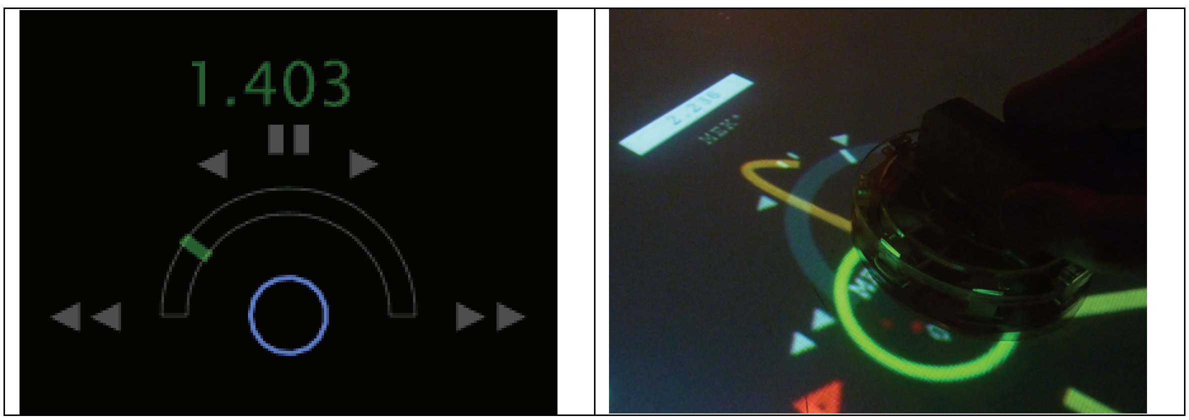


Figure 5-9 The left image is the digital content when a physical dial is pointing at about 10 o'clock. Turning the dial in this direction decreases the number. In the right photo, a user increases the number by spinning the dial toward "▸", which is the symbol for "*forward*".

It is difficult to design tangible interactions that control physical objects that map to digital contents. Systems biologists largely rely on pen and paper. The goal is to create an interface that allows them to continue their regular productive tasks more effectively. Even though there is research showing that tabletop interfaces are effective collaborative tools, some users feel awkward when they first approach the table. Moving an object on a digital surface to reveal further information is uncommon in real life. So is moving an object with one finger. However, we expect the current popularity of multi-touch mobile devices will cause users to grow more accustomed to this type of interface in the future.

5.7 Visualizations

There are benefits and drawbacks to using different types of visualization techniques. One design decision we needed to make was using abstract versus more organic-looking pathways. An abstract visualization [Karp et al. 2010; Ogata et al. 1999] is very similar to a subway map. It gives users a clear overview of the pathways. However, we wanted to make the pathways look and feel more organic. For example, I wanted the molecules move and morph slowly like amoebas. A very structured abstract pathway similar to a subway map looks more robotic than organic. Moreover, I believe an organic look of the system makes it less intimidating to non-expert users then a robotic one.

5.7.1 Reactions

To show the reaction speed, we had several options. One simple solution is to change the stroke weight of a reaction arrow based on its flux, namely the reaction speed. Another similar visualization is to change the arrow color based on its data. However, these two methods do not always generate steady and clear visualizations. When the change is subtle, usually users cannot tell the difference. Another technique that is more perceivable to users is to use animations. The animation requires moving small arrows one by one from one node to another. This might give users clear feedback about the data. Other visualization options include using numerical presentations of flux, using pie charts to show normalized speeds, or using a progress bar to show the values.

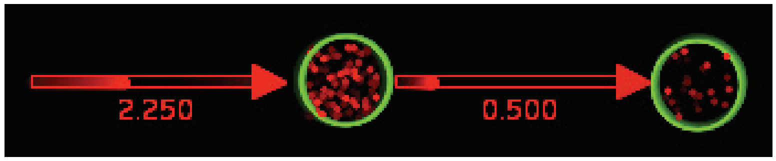


Figure 5-10 The reaction arrows in the first prototype. There is a moving red dot inside each arrow. The red dots in the green circles indicate the concentration of the molecule.

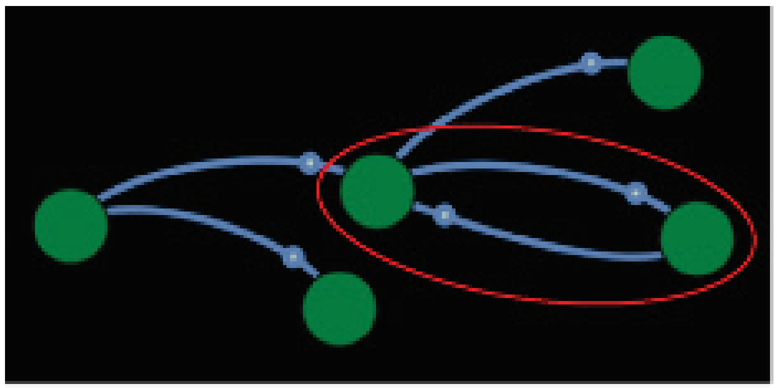


Figure 5-11 A different version of reaction arrows.

The reactions in this figure are modeled by the Bézier function. A small dot is moving from one node to another. The red circle indicates a reversible reaction. Other than the "numerical presentation," all the alternatives have the problem of not being able to reflect the actual data. In other words, users can hardly discern the subtle changes of values. Consequently, our final decision was to use animations to show the speed since they provide the most obvious feedback. However, the animations caused complaints from one user later.

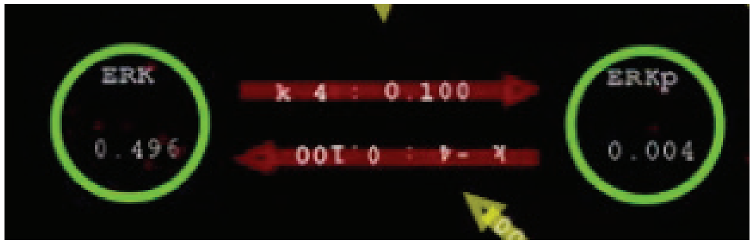


Figure 5-12 The reactions in the second prototype

One common issue with the previous reaction design was the pixels in a reaction, which do not present any data take a large ratio of the entire reaction visualization. The parts (the animating dots) that reflect the real data use relatively fewer pixels. In other words, the data-ink ratios of these designs were low. Therefore, I reduce the stroke width of the reaction. In addition, I redesigned the reactions by adding Bézier curves, which made the reactions look more organic. I also added small arrows moving along the reaction curves. The speed of an arrow reflects the speed of that reaction. The reaction constant is shown on top of the reaction as well. Figure 5-10 to Figure 5-13 show the four different reaction designs.

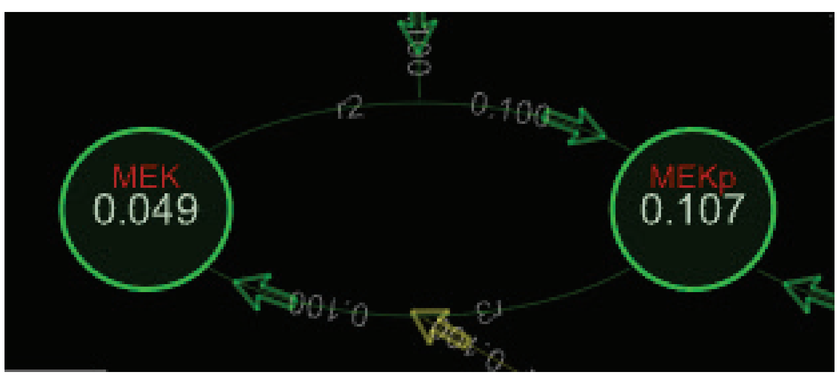


Figure 5-13 The new reactions are made of Bézier curves

5.7.2 Molecules

We changed the size, the filled color, and the stroke color of the molecules based on the concentration value in the beginning but encountered similar problems – users could hardly tell the difference between different molecules. Therefore, we used similar animation techniques to visualize the molecules (see Figure 5-10 to Figure 5-13). The molecules move slowly and randomly in a confined area. They also "breathe" slowly by changing the width of their shape (see Figure 5-14). The stroke color of a molecule shows its type. Green is for molecules and yellow is for enzymes, which is also a different kind of molecule. The higher the concentration value, the deeper the breath a molecule makes. A molecule also has its name and concentration value on it. We added some red dots in one prototype to evaluate the visualization. The dots are generated randomly inside a molecule. The number of dots reflects the concentration of a molecule.

Figure 5-14 An image of three molecules breathing. From their shapes, we can tell *Raf* is exhaling while *Raf and *P1* are most likely inhaling when they were captured.**

5.7.3 Charts

According to Lab G's systems biologists, the chart is the most important information for them to understand a series of reactions under certain initial conditions.

One of our goals is to allow the biologists to work more effectively without frequently switching between charts, ODEs, and the sketched pathways. Therefore, in our application a chart is considered a supplementary tool. Ideally, system biologists will read all the information from the graphical representation of Pathways. Currently, a tangible object is used to control the charts' position.

The charts in Pathways show the concentration changes along the time. In each single chart, the corresponding molecule's name and concentration value at that time are shown (see Figure 5-15). A vertical baseline moves as time passes. A user can compare the concentration values of different molecules at the same time.

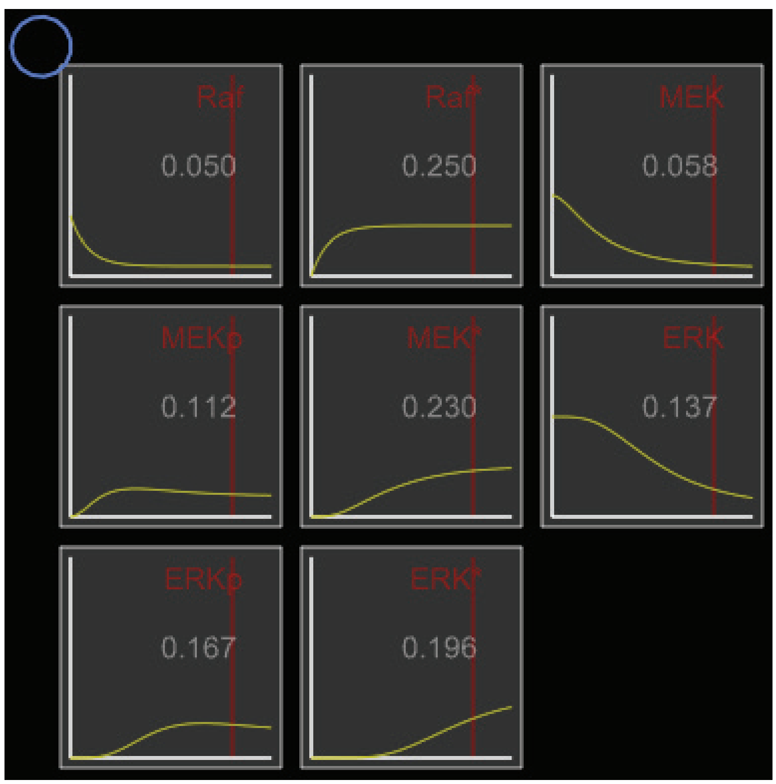


Figure 5-15 The latest output charts of the MAP Kinase cascade pathways. The red vertical line is moving with time to show the concentration at a certain time. The curves are plotted in advance.

5.7.4 Challenges

Within our lab, the system has been iterated several times to find out the most appropriate representation of the simulation and the most straightforward interaction techniques. The feedback from the respondents indicated several challenges in developing such a visualization.

5.7.4.1 A Comprehensible Representation

Since there is no standard for drawing a pathway, every researcher has a different method. Sometimes a researcher chooses a representation based on the modeling method. For example, sometimes intermediates are critical under one modeling method, but are ignored in another modeling method. Also, researchers like to work with a graph that matches their mental model. Two researchers may use the same modeling method and visual representation, but the way they organize the pathway can be very different.

5.7.4.2 The Appropriate Visualization

To make the molecule look organic and life-like, we embedded animations into the simulation. The molecules move randomly in a small confined area, and the shape of the molecule morphs with time. The speed of the movement and the magnitude of the morph are affected by the concentration of the molecule. We particularly exaggerate this effect for users so that they could see the maximum and minimum values of the visualization. We discussed alternative methods for visualizing concentration changes, such as varying the color of the molecule or the thickness of the molecule border, but these techniques made subtle changes hard to notice.

One important topic in information visualization is to maintain graphical integrity [Tufte and Howard 1983]. For example, in a bar chart, if the height ratio of three bars are 1:2:3, the ratio of the underlying data values should be 1:2:3. Using animations in visualization can help users understand the overall distribution of the data but does not show the details unless additional features are added. The animations may need to be exaggerated to emphasize their effect; however, this exaggeration can cause the user to misinterpret the data. Several of the respondents suggested changing the circle sizes of molecules to signify the concentration changes. However, this changing of a two-dimensional area is not a good mapping for the one-dimensional concentration data.

5.8 Application Programming Interfaces (APIs)

The Tangible Tracking Table uses the software engine of reacTIVision. Pathways is built on top of the MT4j framework that receives the data sent from the reacTIVision server. The data packets are in the format of TUIO [Kaltenbrunner et al. 2005], a protocol for tabletop interface implemented using Open Sound Control (OSC) [Kaltenbrunner et al. 2005]. The MT4j framework provides basic APIs for gestural and object interactions on the tabletop. Therefore, Pathways has the zoom, pan and rotation functions that are common to most interactive tabletops. In addition to that, Pathways has its own APIs (see Appendix B) to create biological models. For model creating, current Pathways read models from files. It has the APIs to read a model structure from an Extensible Markup Language (XML) file and display the model on the tabletop. To visualize models, output results, and the fitting process, Pathways includes the Java Classes to create molecules, enzymes and reactions. It also provides the Java Interfaces to apply animations on these visual elements. To enhance the modeling and fitting process, there are APIs to filter to the inputs from the tabletop and generate the output charts, the radar charts and the visual dial. Pathways also includes a math library [Flanagan 2012] to solve ODEs quickly.

There are also lower level APIs designed to intercept and record TUIO packets. Therefore, Pathways records the entire modeling process on the tabletop, including the tangible interactions, finger touches and numerical data of the model. The user can playback the entire process later in different speeds. This log file could be useful for data analysis in user evaluations.

5.9 Current Version

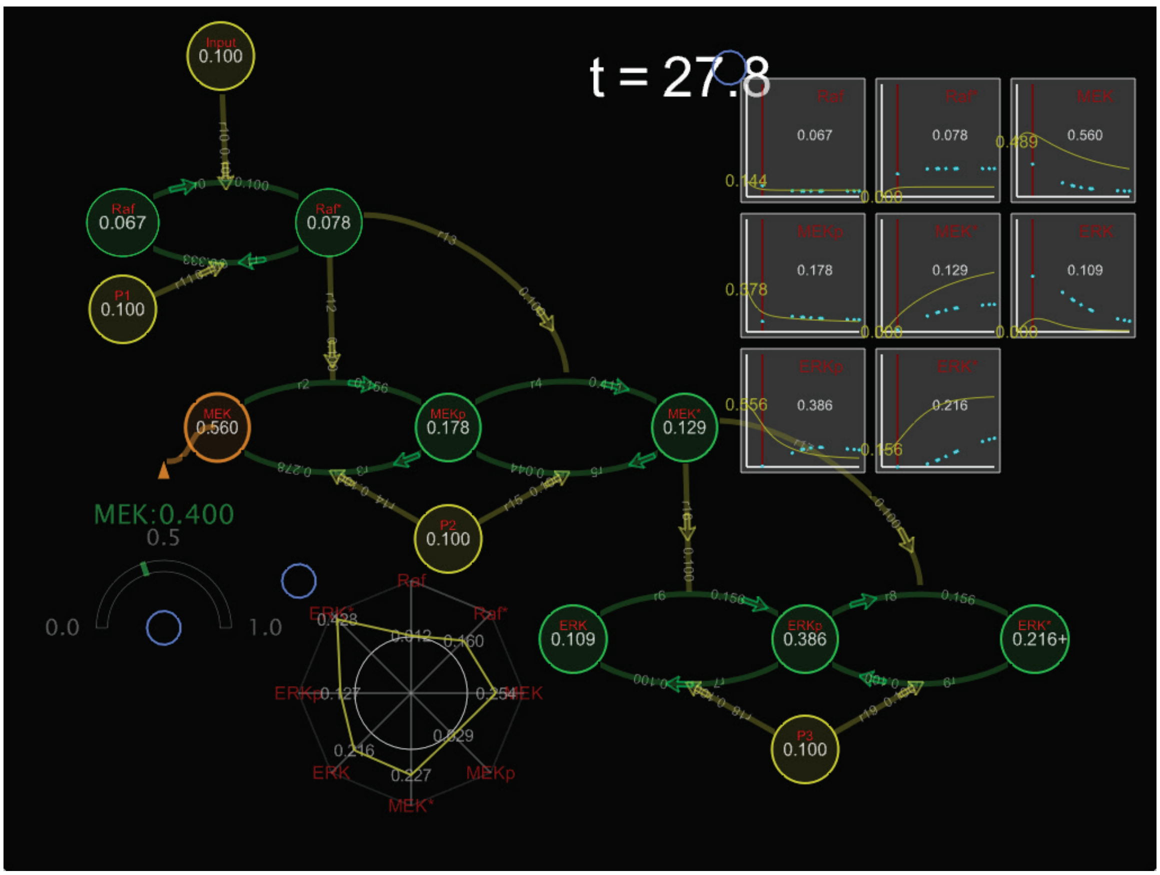


Figure 5-16 A screenshot of Pathways. This is a special edition for user evaluation.

The stable version of Pathways is configured for the evaluation designed to substantiate my thesis hypotheses. Figure 5-16 shows the screenshot of this special edition. During the evaluation, this screen was projected onto the tabletop from a projector embedded in the table. Subjects look at this picture as a tabletop image rather than looking at it on a vertical display. This version of Pathways uses the same color-coding convention as the previous versions. The green circles represent molecules and the yellow circles are the enzymes. The green curves are the regular reactions that are adjustable and the yellow curves are the catalytic reactions, whose reactions constants remain unchanged in the simulation.

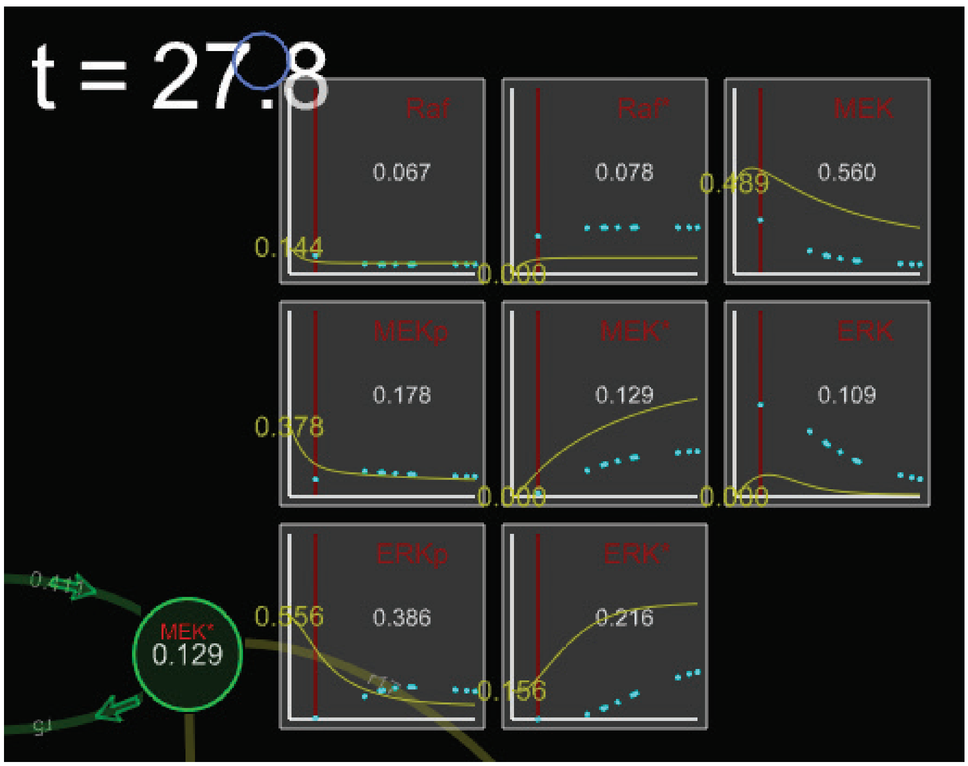


Figure 5-17 The output charts.

The output charts in Figure 5-16 show the simulation results together with experimental data. There are 8 molecules in this model; therefore, the output chart is a collection of 8 charts. The name of the molecule is labeled in dark red on each chart. The x-axis of the chart is the time axis, ranging from 0 to 200; the y-axis of the chart is the normalized concentration value, ranging from 0.0 to 1.0. The vertical lines in dark red are the moving time lines. In this example, all time lines are at t = 27.8. The yellow curves represent the simulation results. The cyan dots represent the experimental data. The yellow number overlapping the y-axis is the initial concentration of that molecule. The white number in the center of the chart is the current concentration value of that molecule, which should be identical to the white number shown in the center of the corresponding green molecule visualization. For example, in Figure 5-18, the current concentration of MEK* is 0.129. One can see this from the chart labeled “MEK*” and the green circle at the lower left of the figure.

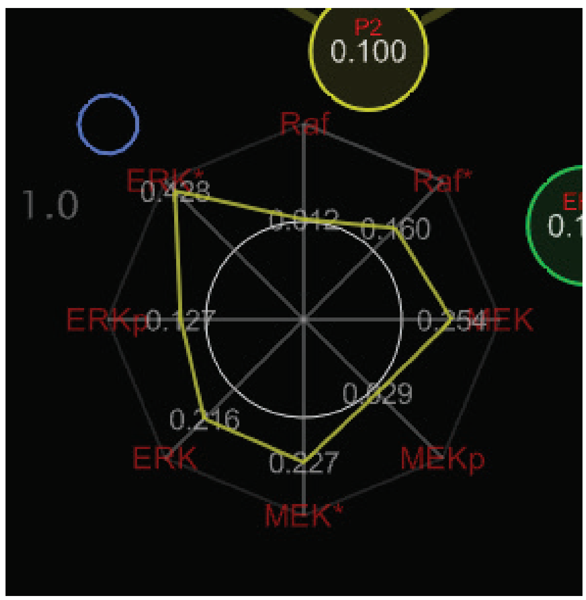


Figure 5-18 The radar chart that shows all RMS error values.

The experimental data is a simulation result of a particular data set. The goal of the task is to find a solution as close as possible to this data set using the tangible controllers and information provided on the tabletop. The cyan dots on each chart are the concentration values of the corresponding molecule at 10 randomly selected time points. The use of sparse cyan dots is based on feedback from one of the systems biologists I work with. Because the experimental data systems biologists get are usually scattered concentration values along a timeline, they usually do not get more than 5 data points on one chart. However, choosing only 5 experimental data points in this evaluation would generate more solutions, which might lead the fitting to trivial solutions that can be easily obtained. Therefore, I picked 10 randomly selected time points to get the experimental data.

The radar chart in Figure 5-18 shows the Root Mean Square (RMS) error values of all molecules. The RMS error value of a molecule is obtained by the following equation:

$$\boldsymbol{X_1} = \begin{bmatrix} \boldsymbol{x_{1,1}} \\ \boldsymbol{x_{1,2}} \\ \vdots \\ \boldsymbol{x_{1,n}} \end{bmatrix}$$

$$X_2 = \begin{bmatrix} x_{2,1} \\ x_{2,2} \\ \vdots \\ x_{2,n} \end{bmatrix}$$

$$\text{RMS error value of } X_1 \text{ and } X_2 = \sqrt{\frac{\sum_{i=1}^{n}(x_{1,i} - x_{2,i})^2}{n}}$$

Equation 5-6

X_1 represents the experimental data and X_2 represents the simulation results. In this evaluation, $n = 10$.

The design goal of introducing the radar chart was to making the comparison of the simulation results with the experimental data faster than the systems biologists' current toolss. I drafted several different types of prototypes to see if users can capture the performance of fitting within a glance. Other candidates included a column chart, and a heat map. I found the column chart was quite helpful for showing all RMS values together as well. However, comparing to a circular radar chart, a radar chart could show more information the same area. Because to increase the information capacity of a column chart, the chart has to extend horizontally, which takes lots of space. A heat map shows the RMS values on a mini map using different levels of colors. It gives the location information that helps user to quickly locate the position of the molecule that requires further tuning. However, when the model grows bigger, the size of the mini heat map has to grow larger, too. Otherwise, the mini map will be too condensed to read. As a result, the data-ink ratio and the scalability had become the two main concerns I chose the radar chart, not the other two options.

The systems biologists' current toolss do not include visualizations that help them read the RMS values effectively. The radar chart gives an overview of all RMS values on one chart. All points that represent the RMS values are connected to form a yellow polygon. In the center of the chart is a white circle, which represents the baseline when all RMS values equal to zero. In other words, the fitting process can be interpreted as changing all adjustable parameters in the model, so that the yellow polygon can be as close to the white circle as possible.

The RMS error value is annotated in white text along the axis of each molecule. In the center of the chart is a circle, which represents the condition when all RMS error values are equal to 0. In other words, the purpose of the fitting process is for the subject to adjust all parameters so that the yellow polygon can be as close as possible to the white circle. In this evaluation, I will evaluate a solution by calculating the average RMS error value of the solution by the following equation:

$$\text{The average RMS error value} = \frac{\sum_{j=1}^{m} RMS\,(j)}{m}$$

Equation 5-7

In a real modeling task, a modeler would modify the equation of the RMS error value and add weights to particular molecules. This is quite common when a modeler wants to concentrate on a particular part of the model.

The output result chart and the radar chart are both controlled by tangible controllers, which can be placed anywhere on the tabletop. These tangible controllers are physical objects with fiducial tags attached underneath them. When these tangible controllers are lifted from the tabletop, the charts disappear. The blue circles in Figure 5-16, Figure 5-17, and Figure 5-18 point out the locations of the tangible controller when the controller is placed on the tabletop. Therefore, the charts are not obstructed by the tangibles.

To change the concentration values of the molecules and reaction constants of the reactions, one can use the dial to select the elements and change the value. In Figure 5-19, the user uses the dial to select the MEK molecule, which turns orange and creates a link between itself and the dial. The design of the dial was changed to the new form based on the feedback from my collaborator. The old dial was design to resemble the dial controller of some old VCRs. Rotating the dial clockwise and making the indicator point at the top right quadrant of the underlying image makes the controlled numerical value start to increase. When the dial is rotated even more in the clockwise direction, the increasing speeds up. The speed reaches the maximum when the indicator is pointed at the rightmost position. One benefit of the old dial was that it allowed users to fine tune the number. However, the biggest drawback was the value could easily exceed the anticipated value. Therefore, the user had to rotate the dial in the opposite direction to reduce the value. A user had to rotate back and forth to locate the exact value. The design of the new dial was intended to solve this problem. Instead of controlling the increase/decrease rate of the number, the new dial was designed to select the value of the number directly. The semicircle distributes values from 0.0 to 1.0 evenly. When one wants to select 0.5, she has to rotate the dial to the middle and lift the dial. Lifting the dial tells the system to restart the simulation.

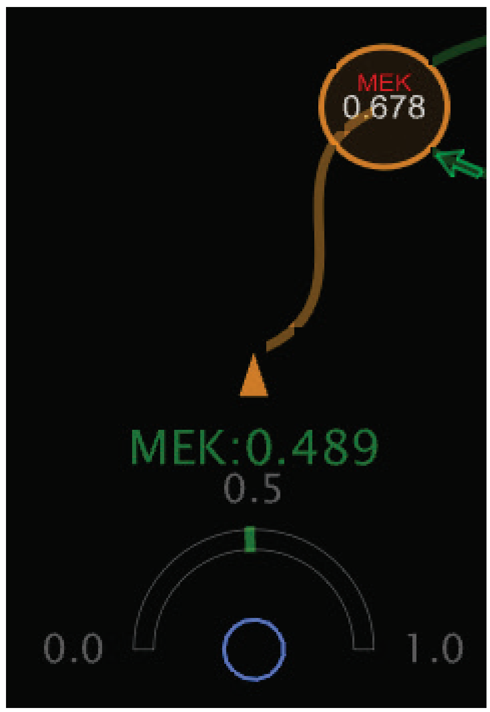


Figure 5-19 **The MEK molecule is selected by using the dial.**

6 Evaluations

There are two forms of evaluations in Pathways, the informal iterative feedback from the researchers from the Biomedical Engineering (BME) Department at Georgia Tech and the formal evaluation I present in this chapter. These two forms of evaluation are both important to Pathways. The iterative feedback from the researchers from the BME department gave my collaborators and me the perspective of the systems biologists. After all, Pathways was designed to improve systems biologists' modeling efficiency. Their feedback was more qualitative and focused on the design of visualizations and the flow of the modeling process. This chapter presents the other form of evaluation, the formal evaluations to gather quantitative and qualitative data. The participants of the evaluations included systems biologists recruited from two BME labs, which concentrate on modeling in the BME department. To further evaluate the usability of the system, we also recruited participants with no biology background or knowledge of modeling in the formal evaluation.

In this chapter, I will present the quantitative and qualitative evaluation results to support my thesis statement through empirical user studies. In particular, I will compare the fitting process for Pathways with the equivalent GUI method.

6.1 Informal Iterative Feedback

I have developed a prototype of Kinesthetic Pathways that runs a predefined model. As this is a system designed to support scientific discovery in a complex area, the available user base is very low (around 10 researchers) and their needs are diverse, so it is difficult to conduct formal evaluations to find out the efficiency of different visualizations. My collaborators have conducted a series of user feedback sessions with individual researchers, and I am using this feedback to develop a new prototype. I expect many cycles of this iteration process before a final prototype is achieved. Here, I present the summarized feedback on the current Pathways prototype.

Users gave me some feedback on the visualization of the simulation. The current prototype does not have the capability of comparing different initial conditions, which is very important to researchers. Such a comparison is part of the fitting process in modeling. Researchers wanted to see the overview of the entire system while having the capability to focus on a smaller region. The older version of Pathways showed the whole system within a fixed view. The latest version of Pathways is zoommable and pannable, which allows users to concentrate on a smaller part. One researcher thought the animation was distracting. What he didn't know, however, was that the animation was adjustable and customizable to individual users. Most researchers agreed that Pathways would be an ideal platform for demonstration and educational purposes.

Some of the researchers could not understand the reactions without the output graphs. Most of these researchers used numerical programming tools to simulate the reactions. The outputs of their simulations were usually the concentration changes of different molecules with different initial conditions. Without the output graph, some of the researchers could not connect the reactions with the model. One of the researchers pointed out that he needed to see the ODEs to understand a reaction. Other researchers were able to convert a reaction to the model without a problem. One researcher wanted to change the topology of the visualization, saying that moving the nodes and curves around would help her connect visualization with her mental model.

The current simulation is generated by the graphical input of molecules and reactions. When a user creates the molecular reaction system, the corresponding ODEs are generated at the same time. One researcher wanted to write the ODEs for the system to generate the visualization and simulation. Other researchers considered the graphical representation as clear as math equations. I obtained the current test model from one of the researchers. It is a model that generates a complete set of results. However, usually the experiment data a researcher obtains contains discreet points rather than a complete set of points that generates continuous curves. This implies that researchers have to go through the modeling process iteratively to find out the best model. Most of the feedback I have obtained is from the system design perspective. The collected data has helped me improve the design of Pathways. My next step will be to make the tangible manipulation of data more intuitive for me to observe the users' reactions. My goal is to show that kinesthetic interaction can provide an effective means for representing and controlling computational simulations such as scientific modeling.

6.2 Evaluation Objectives

The main goal of this evaluation is to determine to what extent I have substantiated my thesis claims, whether or not a special designed tangible user interface on an interactive tabletop may help solve complex problems better and faster than a graphical user interface application. In this study, I chose the fitting process in biomedical modeling as the target to design a tabletop visualization application, Pathways. I expect the strength of manipulating physical objects on an interactive tabletop with appropriate visualization is the direct control of the information and immediate visual feedback that allow users to manipulate the information faster and more efficiently than they can with a GUI application. Also, I believe TUI can help non-experts to do tasks that require professional knowledge.

6.3 The Experiment

The experiment was intended to address these hypotheses:

Hypothesis 1: *Tangible interactions with appropriate visual feedback can provide a practical approach for adjusting numerical values.*

This hypothesis simply states that tangible objects can be used to control numerical values on an interactive tabletop. It has no need for support from statistical data. The task in the experiment involves adjusting up to 18 numerical values to obtain an optimized solution. Therefore, this is not a trivial task that merely changes several parameters to certain values. The successful evaluation of Pathways substantiates this hypothesis.

Hypothesis 2: *Under experimental conditions, tangible interactions with appropriate visual feedback are more effective than the systems biologists' current tools for finding fitting solutions in biomedical modeling.*

The effectiveness of TUI in this experiment can be evaluated by the best result of each individual evaluation and the shortest time to achieve a reasonably good result. The best result in the context of the fitting process can be decided by the lowest Root Mean Square (RMS) error value in one evaluation. Since each modeler has a different standard for judging how good a solution is, there is no absolute norm that can be applied to decide this. I will look at the lowest RMS error value of one evaluation to decide how good the solution is. Therefore, here, "lowest" indicates a relative value for each subject. To determine the shortest time of a reasonably good result, I'll define the RMS error value 0.1 as an evaluation standard. The shortest time is the time when a fitting solution reaches 0.1. I believe the evaluation results will show that TUI is more effective than GUI for adjusting numerical parameters.

In the experiment, I will recruit subjects who have no experience using the tabletop I built. I will compare the fitting results in two different conditions, TUI as the first interface and GUI as the first interface. I believe after some time of practicing, users of TUI can discover better fitting solutions than users of GUI.

Hypothesis 3: *Tangible interactions with appropriate visual feedback provide feasible approaches for non-systems biologists to accomplish tasks that require professional domain knowledge on the fitting process.*

In the experiment, I will recruit subjects with no biomedical modeling background. TUI with appropriate visual feedback helps users better understand the relationship between variables and the effect of changing a particular variable. Therefore, it could make it easier to find a good fitting solution. Verifying this hypothesis does not require that the experiment results show that subjects without a biomedical modeling background can perform adequate or better than subjects with this type of background. Instead, if non-modelers can perform the fitting tasks well enough, I may say that the experiment results support this hypothesis. The implication of this is that modelers can concentrate on creating the model, which requires knowledge of biomedical modeling rather than perform the fitting tasks, which involve just tuning numbers, which most people can do as well.

6.4 Method

I recruited subjects from the Georgia Tech campus and asked them to take part in the experiment. The experiment was to perform the fitting tasks on two different platforms, Pathways and the systems biologists' "current tools." There were also interviews and questionnaires in the evaluation. I present both the quantitative and qualitative analysis in the thesis.

6.4.1 Equipment

The study has two experimental conditions: the tangible interface on an interactive tabletop and the graphical interface. There are 18 parameters for the subject to adjust. They include the initial concentrations of 8 molecules (*Raf, Raf*, MEK, MEKp, MEK*, ERK, ERKp, ERK**) and the reaction constants of 10 reactions (*r1* to *r10*). The enzymes are independent variables and remain constant during the simulation.

6.4.1.1 Pathways

The interactive tabletop display is the Tangible Tracking Table (TTT) I built. The physical dimension of it is 39" (H) x 54" (W) x 44" (L). The dimension of the interactive tabletop screen display is 32x44 inches, and the resolution of the interactive tabletop display is 1024x768 pixels. The TTT can track up to 180 objects at the same time. It can also track at least 40 stable fingertips at the same time. In the experiment, to reduce the load in the training session, I turned off the fingertip tracking function, which meant that when I conducted the evaluations, the Pathways application did not have the functions of zooming, panning, rotating or moving individual visualization elements.

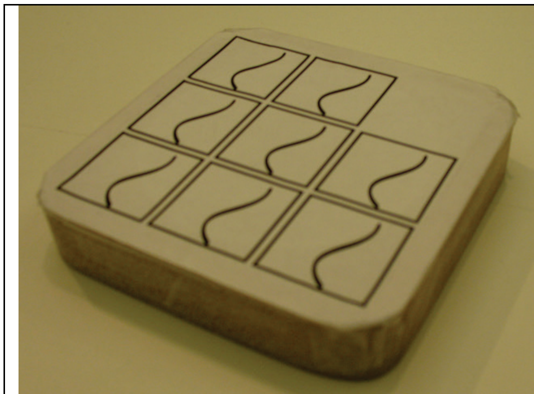
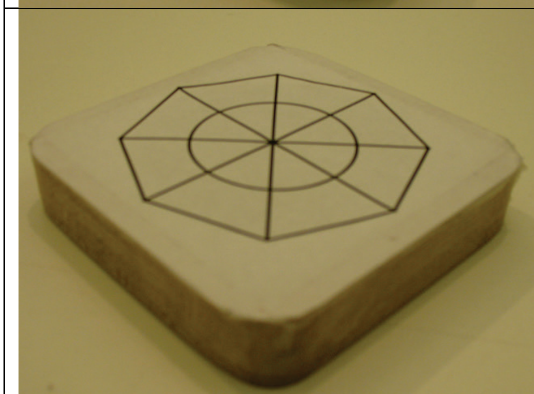
	(a) the tangible for showing the output comparison charts
	(b) the tangible for showing the radar chart
	(c) the dial, the tangible for changing the parameter values

Figure 6-1 The tangibles for controlling Pathways in the evaluation

The three tangible objects are shown in Figure 6-1. Figure 6-1 (a) is the tangible for controlling the position of the output comparison charts. Figure 6-1 (b) is the tangible for controlling the position of the radar chart, which shows the RMS error values of all molecules. Figure 6-1 (c) shows the dial for changing the concentration values of molecules and the reaction speed constants of the reactions. In Figure 6-2, a user is working on the visualization using all three tangibles. This is also the Pathways setting for the evaluation.

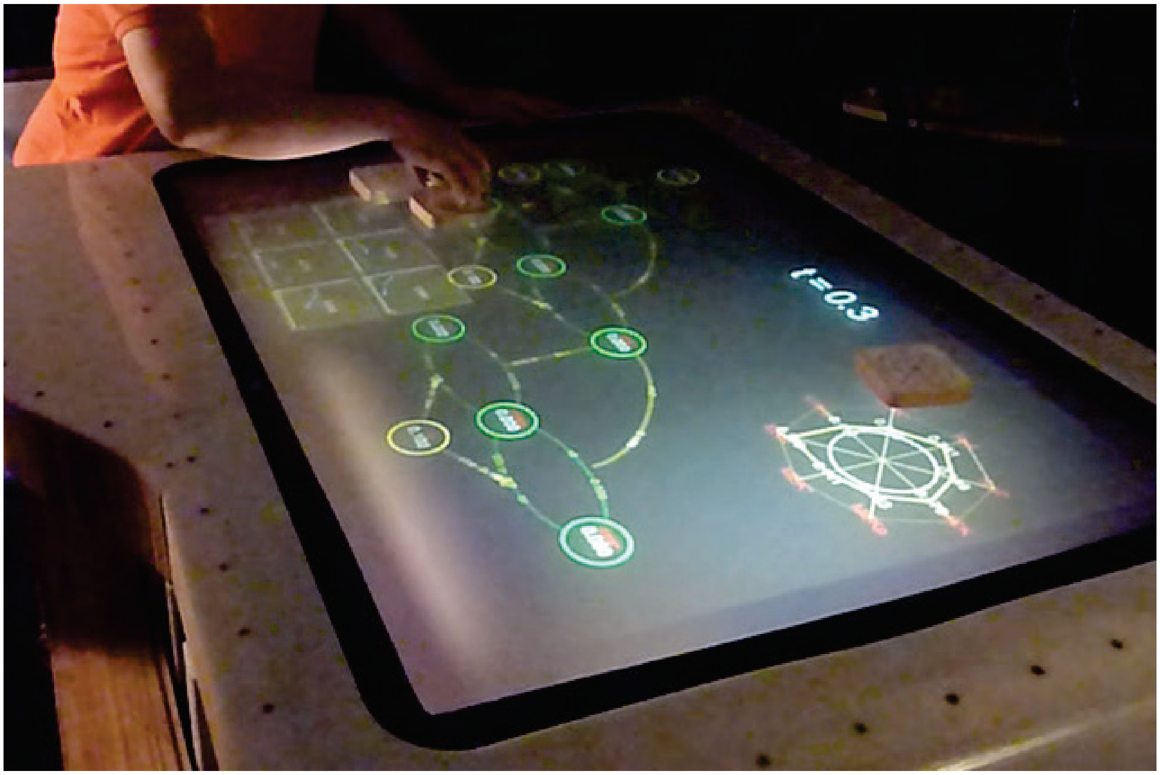


Figure 6-2 A demonstration of all three tangible controllers.

In Pathways, all circles are molecules (enzymes are a kind of molecule), and all curves are reactions. These parameters are the green elements in Pathways. They will turn orange once they are selected. The yellow elements are the enzymes and their reactions. These are the independent variables in the model, and they are unchangeable.

Pathways also uses animations to represent data. The speed of a moving arrow along a reaction indicates the reaction speed of that reaction. When a reaction is faster than another reaction, the arrow moves faster, too. The animation of the molecule also changes with the concentration of the molecule. A molecule changes its radius in the horizontal direction to show its current concentration. The higher the concentration is, the faster the molecule changes its appearance. This animation effect is very similar to a breathing organism.

Pathways was built on the TTT. Therefore, all its inputs are TUIO packages. This special edition of Pathways records all the TUIO packets, including the timestamps, commands, and parameters of the commands. Therefore, I can playback the whole fitting process of a particular user later. It also records important values, such as the RMS error values of all molecules and the average RMS error values when the simulation restarts.

6.4.1.2 <u>The Current tools</u>

The other condition is designed to be similar to systems biologists' current modeling practices. Therefore, subjects were asked to perform the same fitting process using a computer program and a piece of paper with the sketched model on it (see Figure 6-3).

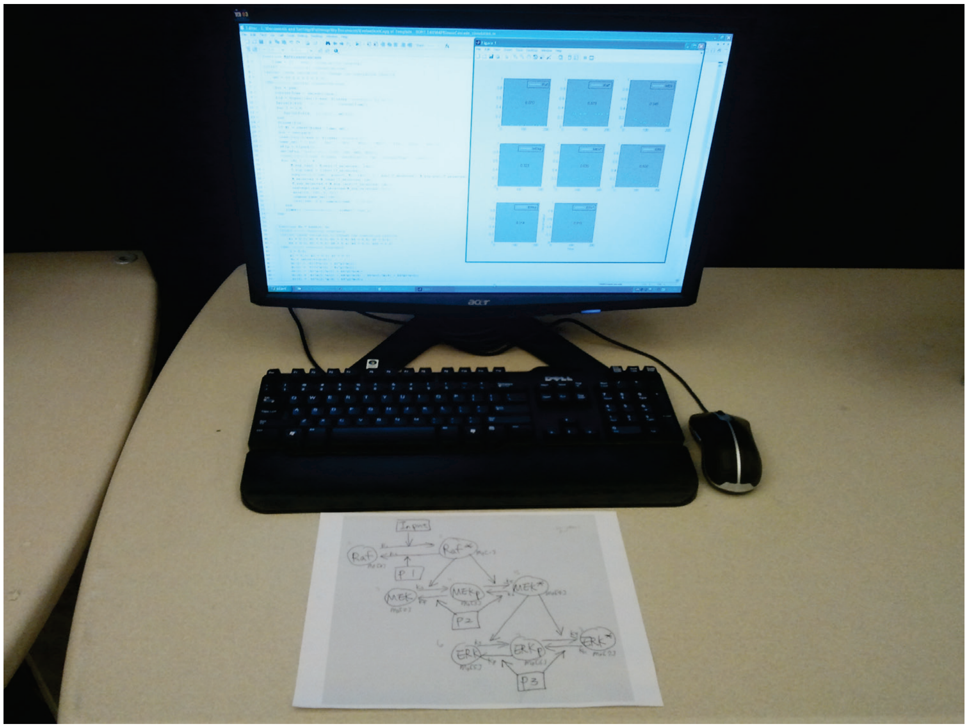


Figure 6-3 The experiment setup for the "current tools" condition.

The computer program that my systems biologist colleagues use the most is MATLAB. MATLAB is good for solving Ordinary Differential Equations (ODEs) with straightforward computer languages and plotting the results. For the evaluation, I wrote a MATLAB program (see Figure 6-4) that solves the ODEs of the same model used on Pathways. In the MATLAB program, 18 parameters are exclusively annotated with comments.

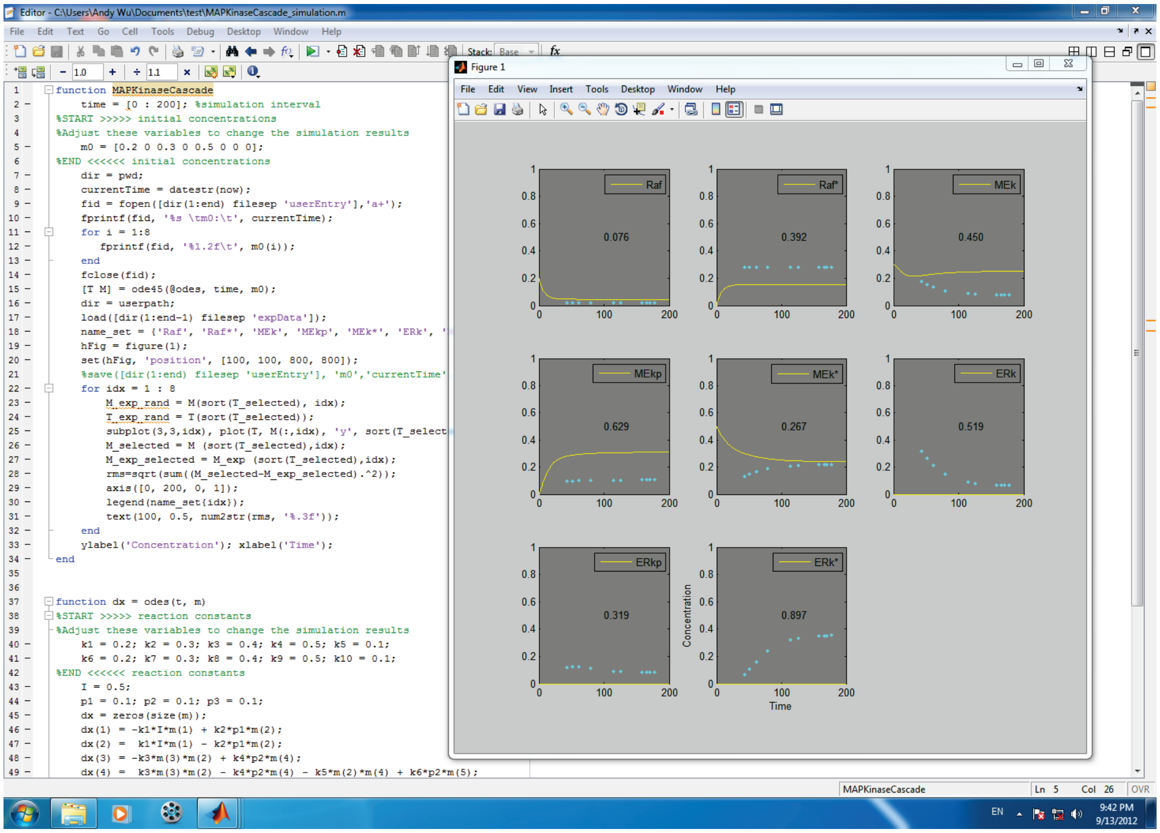


Figure 6-4 The MATLAB screenshot for the "current tools" condition.

Subjects had to change one or more variable values and then clicked the run button at the tool bar to run the simulation. The MATLAB program generated an output chart very similar to the one in Pathways (see Figure 6-5). The name of the molecule was labeled on the chart. The blue dots and the yellow curves represented the experimental data and simulation results respectively. The black number in the center of the chart showed the RMS error value of the experimental data and the simulation result.

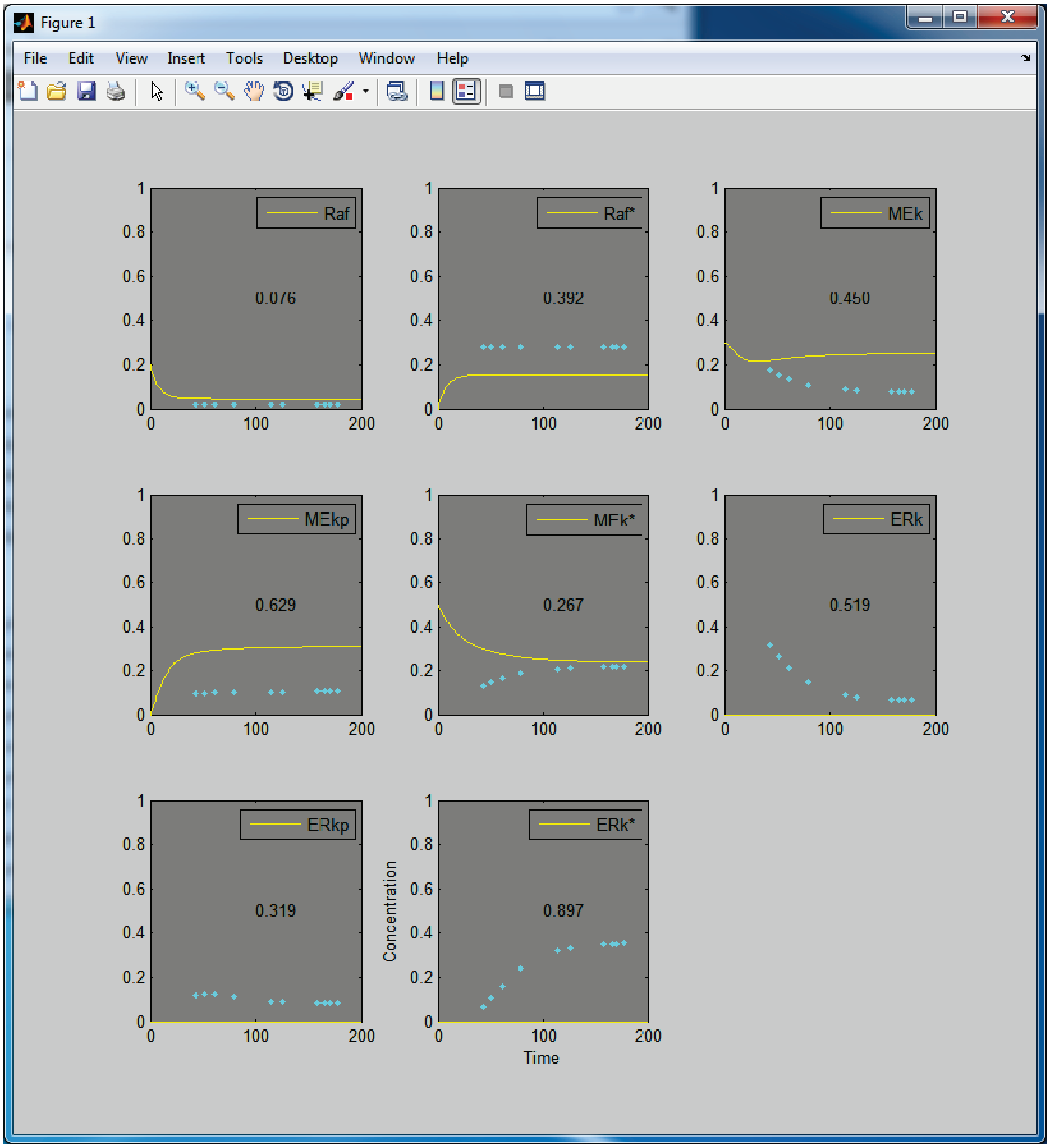


Figure 6-5 The output chart for the "current tools" condition.

A printed sketched model was provided to each subject (see Figure 6-6). The sketch was annotated with comments that linked to the MATLAB program variables. Similar to Pathways, the MATLAB program recorded the input and output of the users.

The recorded data included the timestamp, the RMS error values of all molecules, and the average RMS error value.

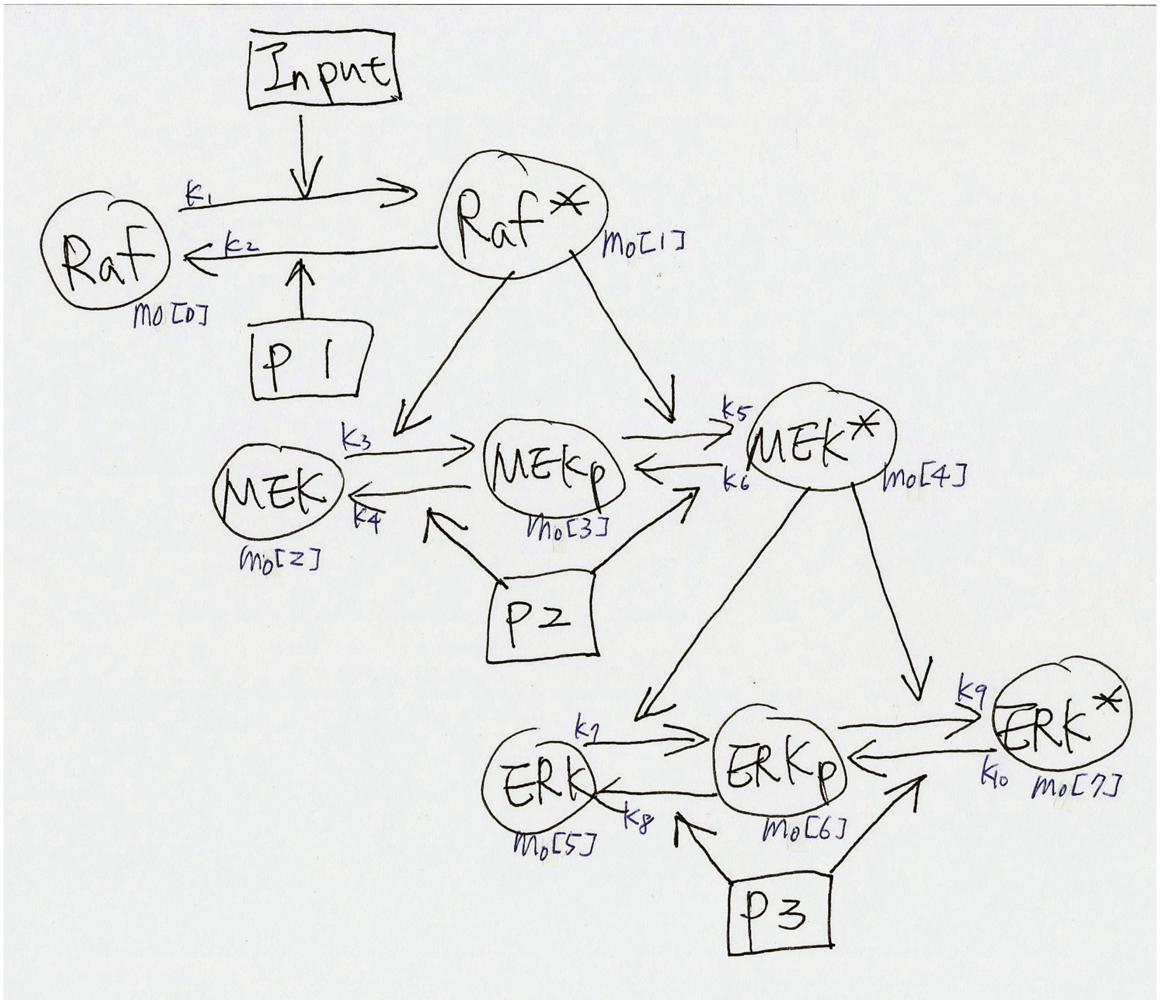


Figure 6-6 The sketched model with annotations.

6.4.2 Tasks

The task was to perform the fitting process and find the best solution possible. My systems biologist colleagues told me that using a simple model like this might take them a few hours to find a good solution. Therefore, I limited the time a subject could perform the fitting task and evaluate the average RMS error values at the end. From the perspective of output charts, the goal was to move the yellow curves as close to the blue dots as possible. From the perspective of math, the goal was to find the lowest RMS error value.

To complete the task with Pathways, the user was asked to stand at the TTT and use the three tangible objects to find the best solution. Because the TTT was built with a projector that requires a dark environment to operate, I turned off the light in the room and left two lamps on to light up the floor.

To complete the task with "the current tools," the user was asked to sit in front of a desktop computer. A paper with the sketched model was placed in front of the computer for the subject's reference. The subject had to use the keyboard and mouse to operate the desktop computer. The light was on during this task.

6.4.3 Procedure

My collaborator and I recruited participants from the Georgia Tech campus. We described our research project and asked them to go through the consent form to see if they wanted to participate in the study. If they agreed to participate, we made an appointment in the lab to conduct the study. Since Pathways was designed to improve the efficiency of the fitting process in systems biological modeling, our subject sets consisted mainly of systems biologists. However, we also recruited subjects from other backgrounds who saw Pathways as a tool with potential to solve other complicated problems in their respective areas in the future. The total amount of time that it took participants to complete their task was 65 to 75 minutes, depending on the subjects' background.

The study began with a 5-minute consent. It had three stages, the *pre-task interview*, *the fitting tasks,* and *the post-task interview*.

Pre-task interview: (5-15 minutes)

- For a subject with a bio-chemical modeling background, there was a 15-minute semi-structured interview, which focused on the current modeling practices.
- For the other subjects, there was a 5-minute semi-structured interview to obtain their background information.

The fitting tasks: (40 minutes)

After the pre-task interview, we counterbalanced the subjects and assigned them unique IDs. Subjects with odd ID numbers were assigned to perform the task on “the current tools” condition first and then switch to the Pathways platform, and vice versa.

- There was a total 10 minutes allotted for the subjects to familiarize themselves with the system and for them to be introduced to the system conceptually. The subjects were introduced to the interface right before they performed the fitting tasks.
- Subjects had 10 minutes to complete the task on each platform. They were allowed to stop if they thought they had found the best solution.

Post-task interview: (15 minutes)

At the end of the study, we asked the subject to fill out a 3-minute Likert scale questionnaire and give 12-minute subjective debrief.

The whole process of the evaluation was videotaped. The (Institutional review board) IRB protocol is presented in the Appendix.

6.4.4 Experimental bias

Following is a list of several experimental biases in the evaluation.

- Most people have extensive experience using keyboards and mice. Four users (see 6.5) had experience using interactive tabletops.
- Users could call "done" whenever they thought they had accomplished the tasks. Even though this is how systems biologists decide the best fitting solution in the real world, it was very subjective.
- Users of Pathways used the triangle in Figure 5-19 to select an element; they lifted the dial to start the simulation. Users of the current tools used the keyboard and mouse to select a molecule or reaction; they pressed the run button to restart the simulation. Changing a value in Pathways to a specific took more time than changing a value in MATLAB since a user had to place the dial on the tabletop to see the position of the triangle and move the dial to select an element.
- The simulation and the update of the output charts in Pathways runs in nearly real-time. The program in MATLAB takes about 1 second to show the output charts. Users of MATLAB don't see the output results immediately. They have to wait for the simulation to complete.
- In the real world modeling, the experimental data systems biologists obtain are usually sparse. For the data of one molecule, there are usually no more than 5 sample points. The experimental data offered in the evaluation provided 10 sample points, which were more than the general cases systems biologists typically face.

- The MATLAB program is quite stable, but Pathways is built on an interactive tabletop prototype, which needs to be manually calibrated before each experiment. Even when Pathways is calibrated, the level of calibration might be different. Trembles could cause the table lose calibration again. In other words, every user experiences a slightly different tabletop detection.
- This is not a comparison between TUI and GUI, but a comparison between systems biologists' current toolss and their experience with Pathways.
- The tangible dial's initial value is based on the orientation of the dial. Most subjects placed the dial on the tabletop in a way that the shape of the dial aligned with the edge of the table. This made the values of the dial to be 0, 0.5 or 1.0. On the other hand, MATLAB users can change the values to arbitrary numbers easily.

6.5 Results

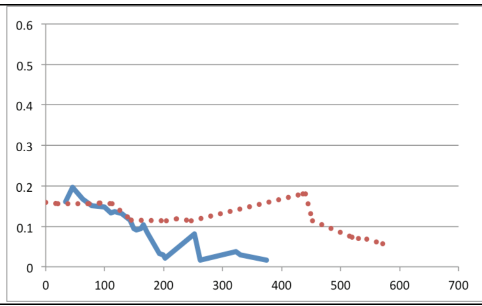
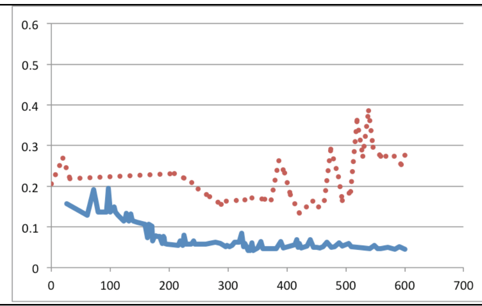
We recruited a total 16 participants. Four of them were systems biologists, who had been modeling for 2 to 6 years. Among all 16 participants, four (user0001, user0005, user0007 and user0012) of them had used interactive tabletop displays before, but only two (user0007 and user0012) are advanced users who had programmed for an interactive tabletop display before. All of them had seen online videos of Microsoft Surface.

6.5.1 The experiment

The experimental data for the Pathways interface was different from the data for the current tools interface. Therefore, subjects could not copy the values they entered for the previous test and apply them to the later test.

The experiment results of all 16 users are shown in Table 6-1 and Table 6-2. The x-axis of the figure in these two tables presents time. The y-axis of the figure in these two tables presents the lowest RMS value. Since the experiments were limited to 10 minutes, all activities in the figures end at 600 seconds. Table 6-1 shows the data collected from users with odd ID numbers, who performed the task on the "current tools" condition first, and then on the Pathways. Table 6-2 shows the data collected from users with even ID numbers, who performed the task on the Pathways first, and then on the "current tools." The systems biologist subjects are user0005, user0006, user0009 and user0014.

Table 6-1 The change of average RMS error values over time for users who performed the task on the "current tools" first. * denotes a systems biologist. Blue solid curves are Pathways results. Red dashed curves are “current tools” results.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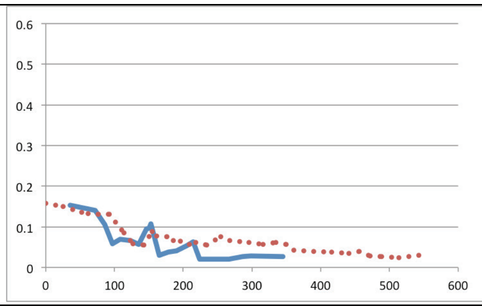	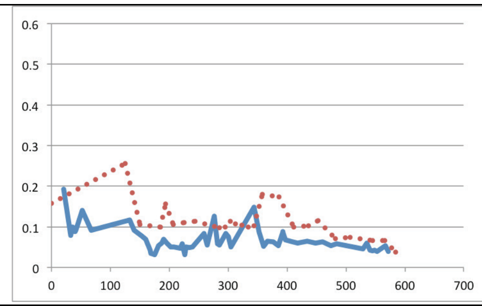
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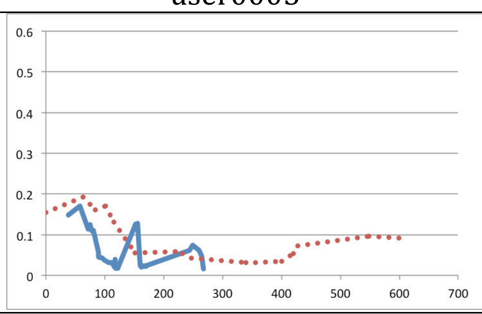	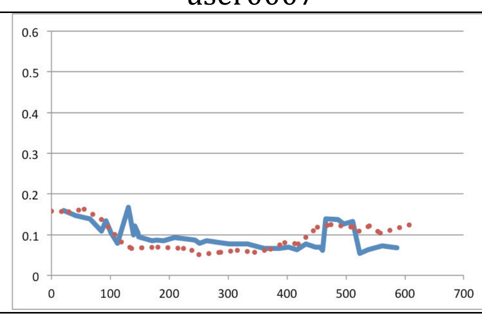
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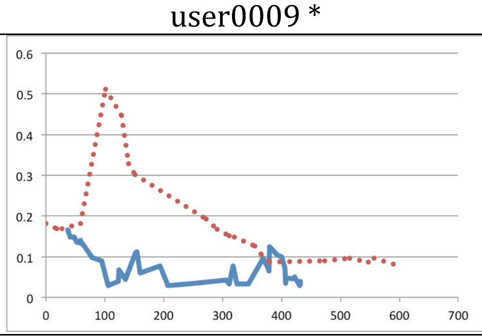
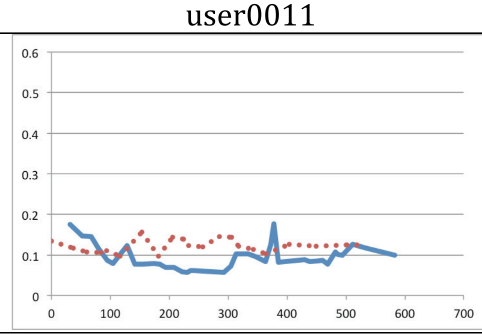
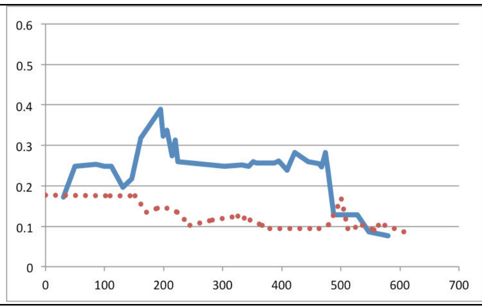
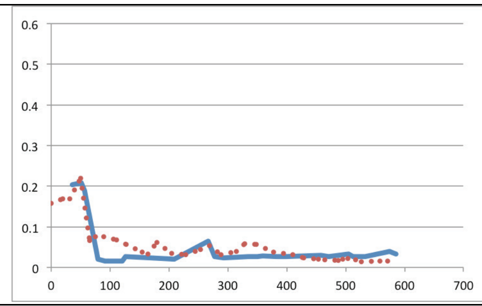
	
user0013	user0015

Table 6-2 The change of average RMS error values over time for users who performed the task on "Pathways" first. * denotes a systems biologist. Blue solid curves are Pathways results, Red dashed curves are “current tools” results.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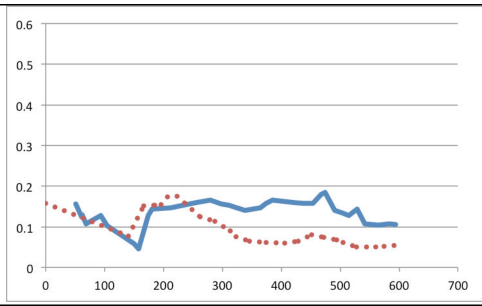	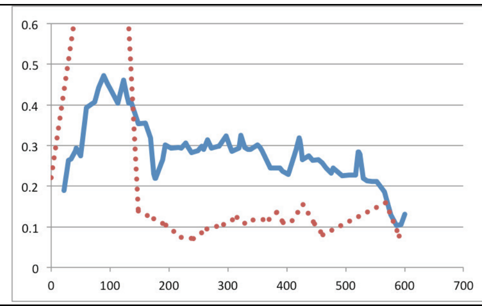
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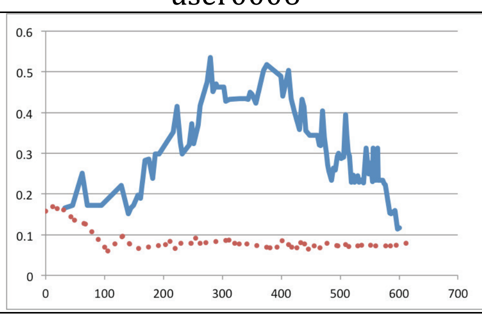
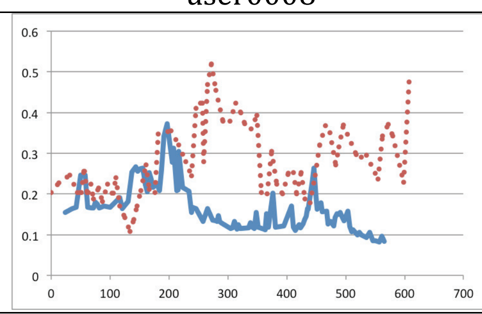
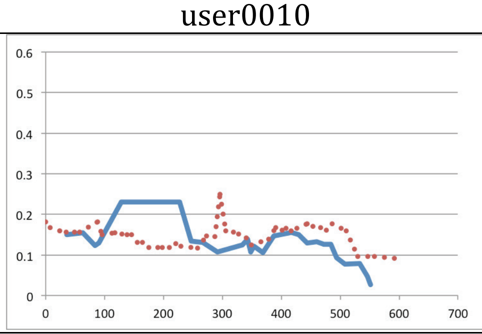
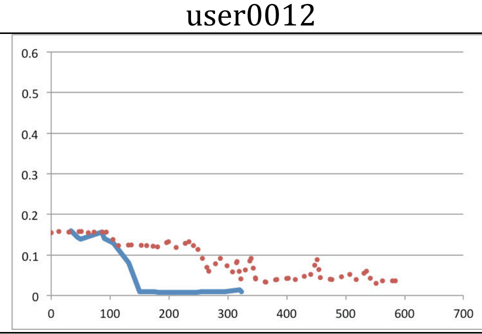
	
user0010	user0012
	
user0014 *	user0016

Inspecting the graphs in Table 6-1 and Table 6-2 reveals the following:

1. Among all 16 “current tools” tests, 2 of them finished before the 10-minute time limit ended. They are tests performed by user0005 and user0015. The subjects finished the task at about 550 seconds or 9 minutes.
2. Among all 16 Pathways tests, 6 of them finished before the 10-minute time limit ended. They are user0001, user0005, user0009, user0013, user0014 and user0016. Most of these subjects finished the tasks significantly faster than the same task in the “current tools” group.
3. The sample points of “current tools” are usually less than the sample points in “Pathways. This is mainly because with Pathways, each modification of a parameter is recorded. In contrast, users can change values of multiple variables before they hit the run button in MATLAB.
4. Several users had achieved satisfying RMS values at some time. But they continued to fine-tune the parameters for better solutions. Therefore, the curve fluctuates slightly after a particular time. A very typical result is user0004’s. He found a very good solution within 100 seconds on both interfaces. After that, he kept trying to find better solutions.
5. Counterbalancing the order in which participants experience the experiment could control the order/practice effect. In Table 6-1, this effect is visible. The Pathways results are mostly better. However, in Table 6-2, the effect is not obvious. I will use statistical data to demonstrate the learning effect in the next section.
6. The changes of the curves in Pathways’ are usually more gradual than the current tools’. This is because in Pathways, one can change one parameter at a time. Therefore, the curves didn’t have steep changes.

6.5.2 Statistical Analysis

To compare the lowest RMS values between the current tools and Pathways, we conducted a paired sample t-test. The test result is shown in Table 6-3. The results show that the mean of Pathways (M = .046) was significantly smaller than that of the current tools (M = .063, $p < .05$). In other words, users overall performed better with Pathways.

Table 6-3 Comparing the lowest RMS values of the current tools and those of Pathways.

	Current Tools	Pathways
Mean (M) of the **lowest RMS values** of all users	0.063	0.046
Paired T-test H0 : $\mu1=\mu2$; H1 : $\mu1>\mu2$ P-value: 0.036		

In Table 6-1, the blue curves are under the red curve in most cases. To compare the learning effect of these two conditions. I separated the samples into two tables: one for comparing the lowest RMS values of all users' first experiments, and the other for comparing the lowest RMS values of all users' second experiments. Independent t-tests were used to compare the two different conditions. The results in Table 6-4 show that the difference in the mean time between the current tools (M=0.062) and Pathways (M=0.059) did not reach statistical significance (p = 0.429). However, comparing the results of the second experiments (see Table 6-5), I found that the mean time of Pathways (M = .0331) was significantly smaller than that of the current tools (M = .0636, p = 0.017). This implies that once users have some idea of what they are doing and understand the basic concept of the fitting process, then the Pathways interface performs better than the current tools, but when they are new to fitting then the interface doesn't make as much difference.

Table 6-4 Analysis of the lowest RMS values of all users' first experiments

	Current Tools	Pathways
Mean (M) of the **lowest RMS values** of all users' **first** experiments	0.062	0.059
Independent T-test H0 : μ1=μ2 ; H1 : μ1>μ2 P-value: 0.429		

Table 6-5 Analysis of the lowest RMS values of all users' second experiments

	Current Tools	Pathways
Mean (M) of the **lowest RMS values** of all users' **second** experiments	0.0636	0.0331
Paired t-tests H0 : μ1=μ2 ; H1 : μ1>μ2 P-value: 0.017		

Another evaluation method is to set a target RMS value, and see how much time it takes for a user to reach this value. In the analysis, I set this target RMS value to 0.1. I found in both conditions that two test results did not meet this target, and their data was excluded. A paired sample t-test was used to compare the time that it took to reach the RMS best solution between the current tools and Pathways. The results in Table 6-6 show that the mean time of Pathways (M = 194.665) was significantly smaller than that of the current tools (M = 235.286, p = 0.046).

Table 6-6 Analysis of the earliest time a test reaches RMS <= 0.1

	Current Tools	Pathways
Earliest **time** (seconds) to reach RMS <= 0.1	235.286	194.665
Paired t-tests H0 : $\mu 1 = \mu 2$; H1 : $\mu 1 > \mu 2$ P-value: 0.046		

Another goal of this evaluation was to see if the non-experts could perform well enough so that they could substitute for systems biologists' to do the work on fitting and reduce the workload of the experts, allowing experts to focus more on tasks that require more professional knowledge, such as creating the model, rather than tuning the parameters. Non-parameter statistics were used to compare the lowest RMS values between experts and non-experts. The results indicate that the difference in the mean time between Pathways and the current tools did not reach statistical significance. However, this is mainly because the sample size of the systems biologists was too small to support the null hypothesis. On the other hand, the M (mean) in Table 6-7 and Table 6-8 did show that systems biologists had obtained lower RMS values than the non-systems biologists. It shows that while both systems biologists and non-systems biologists did better on Pathways, the difference between current tools and pathways was bigger for the systems biologists. It suggests that given more prior experience with fitting, Pathways helps even more.

Table 6-7 Analysis of the performance of the systems biologists

Systems Biologists (N=4)	Current Tools	Pathways
Mean (M) and standard deviation (SD) of **lowest RMS values**	M = 0.049, SD = 0.026	M = 0.027, SD = 0.011

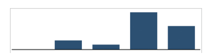
Table 6-8 Analysis of the performance of the non-systems biologists

Non-systems Biologists (N=12)	Current Tools	Pathways
Mean (M) and standard deviation (SD) of **lowest RMS values**	M = 0.068, SD = 0.034	M = 0.052, SD = 0.034

6.5.3 Questionnaire

In addition to the performance measures, subjects also completed Likert-scale questionnaires right after they finished their second experiments. The questions involved comparison between the two interfaces, the use of tangible objects on the tabletop and the feedback of visualization designs. Subjects had to choose a number from 1 (strongly disagree) to 5 (strongly agree). The results are summarized in Table 6-9. The number of subjects for each question is 16, except for the 6th question, which is designed for the four systems biologists only.

Table 6-9 The result of the post-task questionnaire. M is the mean and SD is the standard deviation.

	Question	Sparkline (Q1-5: n=16; Q6: n = 4)	M	SD
1	The tabletop visualization makes fitting process easier comparing with the graphical user interface version.		4.31	0.79
2	I could see myself using the Pathways system		3.69	0.87
3	Using tangibles to control the values is efficient.		3.75	0.86
4	Visualization is not distracting		4.00	0.97
5	The visualization could improve my work or make me better understand the model, the molecules, the reactions and the relationships between them		4.44	0.51
6	[Systems Biologists only] This new fitting process is more effective than my current method.		2.75	0.50

6.5.4 Qualitative user assessments

6.5.4.1 General Observations

All subjects used the paper of sketched model to link between the model and the variables. Everyone used the sketched model provided in the current tools condition in the fitting task. Only one systems biologist subject, user0005, used a pencil to write and calculate on the paper.

Everyone started with molecules first. Most of them noticed that changing reaction constants changed the slopes of the output curves. Some used the reaction constants as the fine-tune tools. All subjects started with the top-left molecules. Because they all notice molecules at the top affect molecules at the bottom.

Fine-tuning variables was difficult on Pathways. 13 people liked the tangible controllers but they also complained about the accuracy of the dial. Furthermore, the value that showed up when they placed the dial on the table was not the parameter value of the selected element, but the value calculated from the dial's orientation. This was particularly a problem when a user wanted to fine-tune a parameter, instead of adjusting the current value of an element, she had to rotate the dial to reach the current value and fine-tune from there.

6.5.4.2 <u>The Interactive Tabletop Prototype</u>

The dimension of the tabletop and the unstable hardware issues affected the efficiency of the fitting process.

- The TTT was obviously too big for subjects who were short. They could not see the image on the tabletop clearly without standing on tiptoe. Even taller subjects sometimes had to lean over the table to see clearly. Some subjects just walked around the table to the other side to place the tangible objects.
- One subject accidently kicked the table after the study and the table immediate lost track of any tangible controllers. In fact, the conditions of the table were slightly different for each test.
- The visualizations were sometimes jittery. Some users had to continuously change the positions of tangibles to find the sharpest visualization.
- 5 users wanted the simulation to restart every few seconds without removing the dial from the tabletop. One user actually experienced this unexpected function because of

the system’s glitch. The table was not calibrated to its best state when this subject tested it. It lost track of the dial quite frequently, and the simulation restarted whenever the system lost the position of the dial. It gave the user the experience of real-time simulation that other subjects were looking for.

- Another complaint was the stability of the table. The table uses two mirrors supported by 4 hooks to create a 55” projection image. Any sudden movement of the table could shift the positions of the mirrors, which made object detection problematic. When this happened, either the table couldn’t detect the controllers or the table thought the controller was at a slightly shifted position.

The four systems biologist subjects used visualizations in their current tools. Three of them use 2D line charts, which are very similar to the output charts in Figure 5-15, to show the changes of molecule concentrations over time. One systems biologist’s work focuses on network analysis, which is the study of how individual cells interact with each other. He uses 3D visualization tools to visualize the positions of cells in the space.

To create the initial models, two more junior systems biologists read the literature to decide on a structure that was as simple as possible. After that, the difficult part was to find out the initial conditions for the optimization algorithm. More senior systems biologists could assign these values based on experience. Some systems biologists used the Monte Carlo Method, which was to let a computer program randomly decide the initial conditions. They anticipated that Pathways could play an important role in deciding the initial conditions for them since Pathways could help them quickly find some good candidate solutions.

One systems biologist stated, "Fitting is not science; it's art." Systems biologists use literature reviews and optimization algorithms to make this process more systematic and scientific. But they still have to experience the non-logical part of assigning initial values.

Three systems biologists wanted the optimization function on Pathways. Pathways could help them find good solutions in a short time, but it could not find the best solution for them. One systems biologist commented, "I think that's a very good system for teaching or for initial steps of the research. If I have no idea about the biochemical system, then I will use the pathways system because I can briefly see the reactions and I can tune everything I want. But after that for the kind of knowledge I need, maybe I will still go to the desktop. The reason is that I may need the optimized output, and other detailed functions."

One systems biologist thought it would be useful for both demonstration and solving real world tasks, but he did not think the final solution would come from that interface. This would be something he uses to see if things work before he writes a computer program.

One systems biologist will use it to solve real world tasks if the output of MATLAB can be the input of Pathways and the output of Pathways can be directed into MATLAB. Then, she would use Pathways to find the initial conditions for optimization and fine-tune the parameters after finding some optimized solutions.

6.5.4.3 <u>Pathways</u>

General feedback for Pathways:

- Two systems biologists wanted to see the ODEs, but Pathways did not have this function yet. Seeing ODEs helps them understand the model better. For example, increasing the concentration of one molecule may also increase the concentration of another molecule.
- The selector (the orange triangle) of the dial always points upward. Some users wanted it to be in other directions, so that they could easily select elements at the edge of the tabletop.
- Some wanted to be able to rotate the graph and the charts to face a certain way
- Pathways could not show values of the Y-axis in the output charts.
- Pathways did not allow the initial concentration to be assigned to any level other than 0. However, assigning some random initial concentrations could make the fitting a little faster.
- Rather than the way the graphs are shown currently, some users would like to choose which graphs they wanted to display.
- Some wanted zoom-in, rotation, and pan functions. In fact, Pathways had all of these. I just disabled them to simplify the interaction in the evaluation.
- Showing the output charts next to the corresponding molecules. In fact, users can move the chart to different locations. I disabled this function to simplify the interaction.
- In the open question, “What did you think was the best feature of the system?”
    - 3 users said it was the tangible controller - twisting the object to adjust the value and lifting it to see the results
    - 12 users said it was the visualization; among them, 3 pointed out specifically the radar chart visualization
    - One user said it was the immediate feedback of the system - seeing everything with the visualization when they adjusted parameters

6.5.5 Strategies

Most users used the same strategies to adjust the parameters of the molecules under two conditions. They usually started from the top row, tried to find the solution for the molecules, and then went to the next row and then the third row. This is a fairly reasonable strategy, since the top row could affect the lower rows, but the lower rows could not affect the top row. One subject (user0008) set all molecules to 0 first and then set all of them to 1 to see the changes between them. After that, she focused on the graphs that were still off and started changing values accordingly.

From the interviews, I believe one intermediate level systems biologist (user0005) had the best strategy to tackle this particular model. He explained to me that this is a balanced model with several reversible reactions. The concentration summation of a balanced reversible reaction should remain constant at all times (see Equation 5-4). Therefore, the concentration sum of *Raf* and *Raf** in Figure 6-6 should be constant at all times. Applying this rule to other parts of the model, we can conclude that *MEK* + *MEKp* + *MEK** is constant and *ERK* + *ERKp* + *ERK** is (a) constant, too. This means he could achieve a very close estimate on the initial concentrations of one reaction. With this type of reaction, the ratio of reaction constants K_1 and K_2 in Figure 6-6 should be constant at all times as well. In a more complicated reaction involving 4 reaction constants, there is a more complex relationship. Therefore, he adjusted only half of the reaction constants to approach the experimental data. These two rules gave him a great advantage in the fitting process. The other 3 more junior systems biologists did not have this knowledge. However, one non-systems biologist (user0004) discovered the first rule when he started to play with Pathways. He obtained very satisfying results (0.015 average RMS on Pathways at 91.46 second and 0.033 average RMS at 164 seconds) in a very short time on both conditions. User0004 had knowledge of basic chemistry and physics. He believed that the energy conservation rule might apply to the chemical reactions, but he was not sure until he started to tune the parameters.

6.5.6 User comments

Subjects offered the following comment on the usage of Pathways:

- "I will definitely use the Pathways system for demos. I will use it for real tasks if it included an optimization feature."
- "I can definitely foresee this being used for something like demonstration, for showing the results to a large audience."
- "Pathways is a visualization of different equations".
- "I liked that everything was connected and I could see what was interacting with what else, compared to GUI. I really like the idea, as I could see what is increasing and what is decreasing."
- "I like the ability to see everything at once. Seeing the graphs along with the molecules, RMS values."
- "I loved the RMS diagram. That and the auto updating were really great. To change the parameters to see the changes reflected in the graphs was great." (In fact, the auto updating was a glitch.)

6.6 Discussion

This session presents the verification of my hypotheses and the feedback from systems biologists.

6.6.1 Evaluation of Hypotheses

The experiment was designed to evaluate these hypotheses:

Hypothesis 1: *Tangible interactions with appropriate visual feedback can provide a practical approach for adjusting numerical values.*

This claim is supported through the successful execution of the study. In the evaluation, 16 users used the tangible objects to adjust numerical values for 833 times. The action involved continuously placing the tangible dial on the tabletop, moving the dial to select a particular molecule or reaction, and rotating and elevating the dial to set the values and restart the simulation. Moreover, 11 out of 16 users agreed or strongly agreed that using tangibles to control the value is efficient (See question 3 in Table 6-9).

Hypothesis 2: *Under experimental conditions, tangible interactions with appropriate visual feedback are more effective than the systems biologists' current tools for finding fitting solutions in biomedical modeling.*

The effectiveness in this experiment can be evaluated by determining the best result of each individual evaluation and the shortest time to achieve a reasonably good result. The best result in the context of the fitting process can be decided by the lowest Root Mean Square (RMS) error value in one 10-minute evaluation. Table 6-3 shows statistical evidence that the Pathways interface helped users find better solutions than the current interface. To determine the shortest time of a reasonably good result, I defined the RMS error value 0.1 as successful. Table 6-6 shows that Pathways users spent less time to reach RMS < 0.1 than users of the other condition.

The subjective feedback from the post-task questionnaire supports this hypothesis as well. Table 6-9 shows that 15 out of 16 users responded agree or strongly agree to Statement 1, “The tabletop visualization makes fitting process easier comparing with the graphical user interface version.” User0012 responded, “disagree” this statement. He was more frustrated while using the tabletop than using the other one because the table was not in the best-calibrated state when he used it. Table 6-9 also shows that all 16 users agreed or strongly agreed with Statement 5: “The visualization could improve my work or make me better understand the model, the molecules, the reactions and the relationships between them.” The subjective feedback is more strong evidence that supports this hypothesis.

Another interesting finding in the experiment was revealed when I compared the lowest RMS values of all of the users’ first experiment in Table 6-4. The results show that there was no significant difference between the two conditions. However, by comparing the lowest RMS values of all the users’ second experiment, I found that Pathways users delivered considerably better solutions than those of the other group (see Table 6-5). The statistical evidence suggests that after the 10-minute fitting exercise, the users understood the problem better than they did after the first test. For the second test, they performed much better with the TUI than with the GUI. However, this particular discovery requires more evidence and evaluation to make any further conclusions.

Hypothesis 3: *Tangible interactions with appropriate visual feedback provide feasible approaches for non-systems biologists to accomplish tasks that require professional domain knowledge on the fitting process.*

In the experiment, 12 subjects did not have biomedical modeling background. The descriptive statistics results in Table 6-7 and Table 6-8 suggest systems biologists outperformed other users. Since the average lowest RMS values of these users are 0.068 and 0.052 for the current tools and Pathways respectively. However, these are the records of all non-expert subjects. Among the 12 non-expert subjects, 3 of them had lower RMS values than the systems biologists' average, which was 0.27. One interpretation that could be made is that these subjects could be candidates to replace the systems biologists as the workers who carry out the tedious fitting processes that the systems biologists can focus on tasks that require more professional domain knowledge. To show the individual user improvement when using the tangible user interface, I created another table (see Table 6-10) to compare the difference between Pathways and the current tools results for individual non-systems biologist users. Each sparkline chart shows the difference between the performances of six non-systems biologists on two interfaces. The dark olive green sparkline represents users who tested the current tools condition first (user0001, user0003, user0007, user0011, user0013, and user0015) and the dark orange sparkline represents users who tested the Pathways condition first (user0002, user0004, user0008, user0010, user0012, and user0016). For example, the second bar in the dark olive green sparkline (user0003) shows that the lowest RMS value of his first test is higher than the lowest RMS value of his second test. In other words, he did better in Pathways than in the current tools. The table shows that even when considering the order effect in the second row of the table, the subjects still obtained better solutions with Pathways than with the current tools.

Table 6-10 Comparison of the lowest RMS values of non-systems biologists in their two tests

Non-systems biologists' test results	sparkline chart (positive bars: 2nd condition result is better than the 1st condition)
1st condition: current tools, 2nd condition: Pathways $\begin{array}{r} \text{lowest RMS}_{\text{1st condition}} \\ -\quad \text{lowest RMS}_{\text{2nd condition}} \\ \hline \textit{the RMS difference} \end{array}$	
1st condition: Pathways, 2nd condition: current tools $\begin{array}{r} \text{lowest RMS}_{\text{1st condition}} \\ -\quad \text{lowest RMS}_{\text{2nd condition}} \\ \hline \textit{the RMS difference} \end{array}$	

6.6.2 Feedback from Systems Biologists

In general, the systems biologists think Pathways is an innovative way to solve problems. All four systems biologists gave neither agree nor disagree or disagree in question 6, "*this new fitting process is more effective than my current method*." However, they gave an average of 4.0 on questions 1 to 5. From the follow-up interviews, we know that there are several reasons they thought the new fitting process is not more effective than their current toolss:

- Pathways has only one predefined model now; its current state is more like a demonstration application, not a tool for solving real world tasks.
- Even though they performed better on Pathways than on MATLAB, the subjects still preferred MATLAB because it allowed them to write their (own) programs and apply different algorithms.

- Pathways lacks certain optimization functions.
- Pathways cannot load or edit models. It does not have the fundamental functions to be a useful tool even though the systems biologists think some of its concepts are brilliant.
- For this particular task, this is not the way some subjects would solve it. Because using the fitting method in the evaluation does not guarantee best solutions, they would write a program using some optimization algorithm to find out the solutions. It would probably take one or two hours to finish.
- Pathways uses only one math model to simulate the reactions. There are several different types of math models (that could be used).
- They loved the radar chart. They did not expect that a simple visualization could significantly improve the way they perceived the RMS values.

7 Discussion

In this thesis, I present Pathways, a tangible tabletop visualization application that helps the fitting process on modeling biological systems. I conducted the evaluations to compare Pathways with the systems biologists' current tools. The results showed that Pathways was more effective. Moreover, Pathways helps non-experts perform fitting tasks that used to be for professional systems biologists only. This chapter discusses other aspects of Pathways.

7.1 Design alternatives

I changed the design of Pathways several times based on the feedback of the users. Some of these changes proved to be the right choices but some proved not to be successful. In this section, I will discuss the possible design alternatives.

7.1.1 Tangible Interaction

Several users liked the use of tangibles, but they also complained about their interactions with it. During the pilot test, a subject suggested that the dial should reflect the absolute values based on the orientation of the dial. Therefore I changed the interaction of the dial according to his suggestion. However, this change did not receive positive feedback during the evaluation. One reason was that the users preferred to align the dial with the edge of the table. This made the values of the dial be 0, 0.5 or 1.0. The other reason was that users wanted to fine-tune the parameters. The new dial design gave a value that had no connection with the current selected value. Therefore, the interaction was not straightforward. From the evaluation feedback, I will change the behavior of the dial to the previous type. The selection of a molecule or reaction using the dial was still difficult since users had to place the dial on the tabletop and move the triangle to touch an element. Since the size of the fiducial cannot be any smaller on the TTT, an alternative way to select and adjust a parameter on TTT is to use a finger or a pen to select an element, and then place the dial to change the value. An improved version of the previous dial would allow the dial to spring back to the "no change" position the way a VCR dial does. I think the lack of that feature was probably what caused people to complain about the initial dial – it would move forward, but not spring back, so you had to turn it back to the start position, but if you overshot a bit (which happens easily because the sensing is not perfect) then the numbers start to go in the other direction. So increasing tracking accuracy/precision and having the spring back function would probably make the first version of the dial work better. Tablet computing has become popular recently and it is more accessible than it was when I started my research. Another application of using finger and gestural interactions is to implement a different version of Pathways that allows changing numerical values through touches. I foresee an Html5 version of Pathways that can be deployed on most common mobile platforms.

I disabled all finger touches and gestural interactions of the TTT during the evaluation because the finger touch detection could begin to flicker sometimes and I wanted to reduce the controlled variables of the experiment, yet, from the evaluation results, the interaction seemed necessary since several users reported that the molecules and reactions located at the bottom of the screen were difficult to select. Figure 7-1 shows a screenshot of a finger gesture enabled edition. In this edition, a user moves some of the output chart next to the corresponding molecule. Because the whole model is too big, the user scaled the model to be smaller than its original size. She also rotated the model because this better fit her standing position at the table.

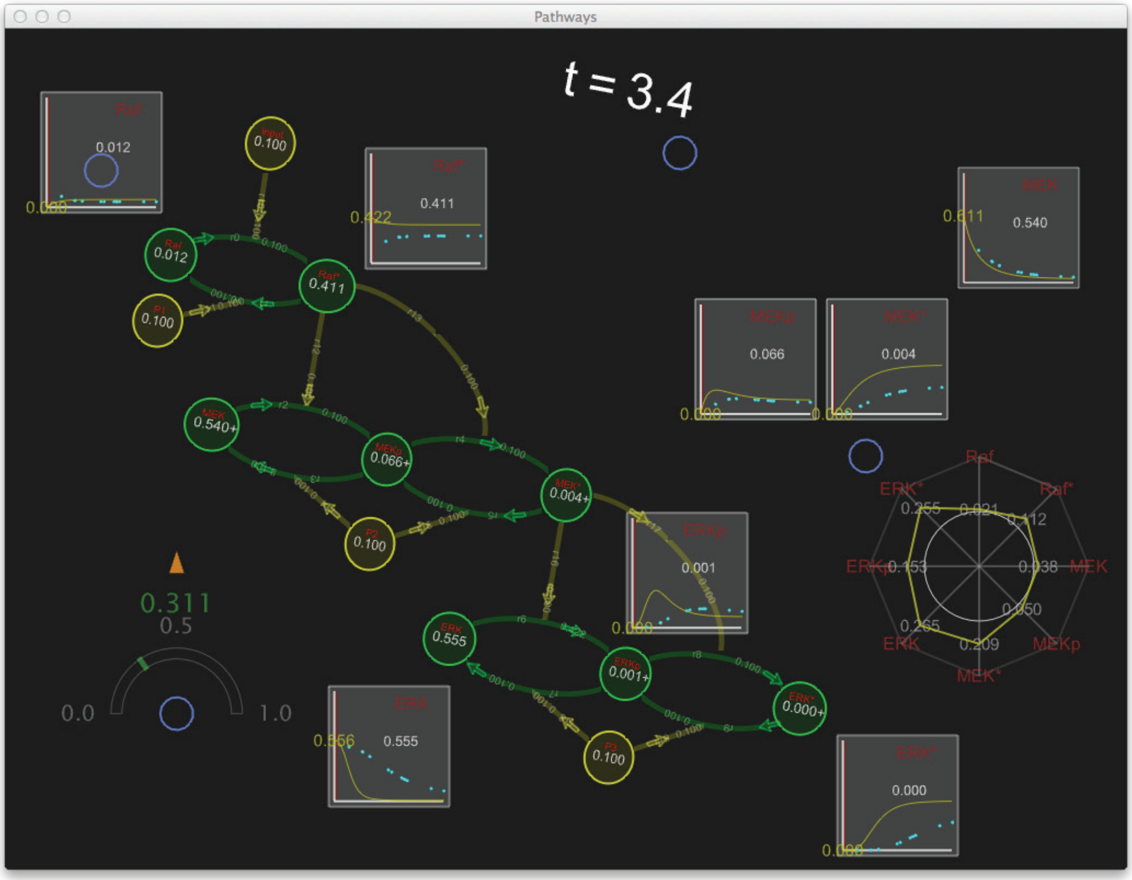


Figure 7-1 Pathways with finger gestures enabled

Synlab bought a new Microsoft PixelSense tabletop [Microsoft 2012] a few months before I started my evaluation. This tabletop is smaller (40”) but has very accurate finger touch detection. It can also detect tagged objects that are as small as 1cm x 1 cm. Ideally, Pathways can be ported to this platform. The sizes of the tangible controllers can be smaller and the detection will be more stable. However, Pathways was programmed in Java, which is not supported by the PixelSense APIs. Therefore, in order to run Pathways on the new table, I need to create a middle ware to convert PixelSense data to TUIO protocol.

7.1.2 Visualizations

Current Pathways loads one predefined model and visualizes it with a fixed structure whose individual elements are not movable. During the second prototype stage a systems biologist wanted to rearrange the model. This is doable in the current Pathways program. However, it was difficult for most users to maintain a clear visualization after a relocating most elements on the screen. Because Pathways was built on top of MT4j, Pathways has 3D visualization capability. Everything we see on the tabletop is actually on a plane in a 3D space.

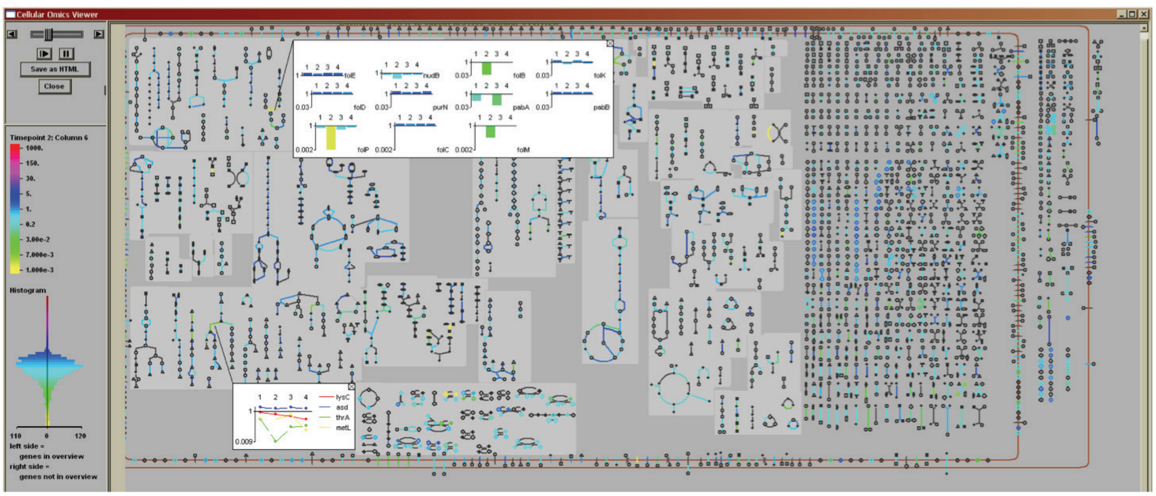


Figure 7-2 Pathway/Genome Navigator in the Pathway Tools

In the design of the visualization, I attempted to make the molecules and reactions look more organic. However, this attempt seemed to be more meaningful for demonstration or educational purposes. An alternative is to make the molecules and reactions look more abstract. The screenshot of the Pathway/Genome Navigator in the Pathways Tools in Figure 7-2 (a) shows an abstract visualization of a pathway. In this visualization, the pathway is represented with circles, triangles, squares and other simple shapes. It gives the users an overview of the pathway using abstract animations. When a user clicks one element, a window pops up to show the detailed information about it. The Cell Designer in Figure 7-2 (b) presents pathways in a more diagrammatic way. Additional information of the pathway is shown in surrounding information boxes. A user moves between the visualization and the supporting information boxes to manipulate the pathway. This is a typical GUI design - selecting an object on the main screen and modifying its properties in a separate window.

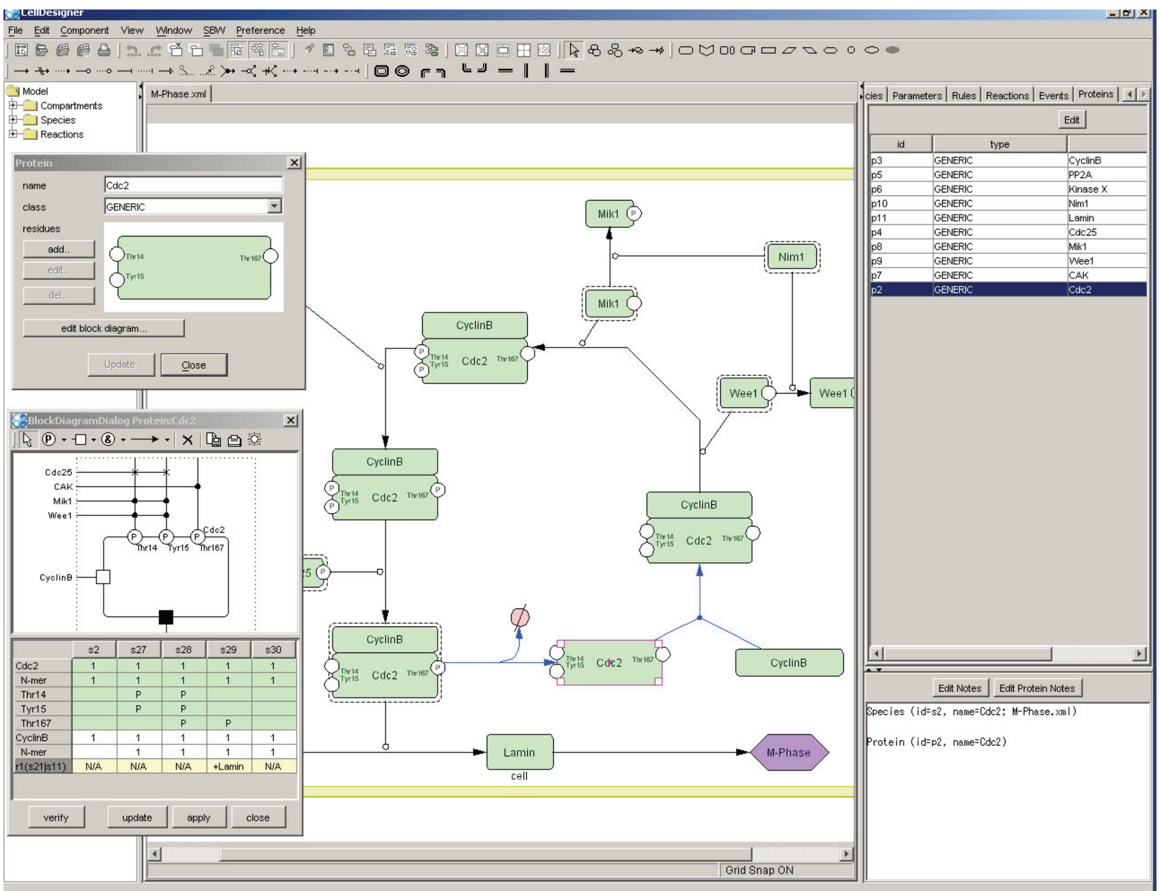


Figure 7-3 The Cell Designer screenshot

Since there were no alternative visualizations for the subjects to comment on in the evaluation, I could not find out which visualization was more favorable to the users. I believe different visualizations should be created for different purposes. For a modeling task, the visualization should be more informative with supporting ODEs, or links to a database of the molecule. To demonstrate a pathway to people with less training, current Pathways can provide clear animations and changes for each molecule. Annotations to the molecules might be helpful but should not be the focus.

7.2 Contributions

1. **A new fitting approach that employs tabletop tangible interactions with visual feedback**

The iterative design process of Pathways and the new fitting process are documented in this thesis. The source code of Pathways archived in an online repository. There are ongoing changes on the Pathways prototype. Research proposals based on the Pathways prototype are submitted for future exploration.

2. **Evidence to support the use of tangible tabletop interaction in modeling biological systems**

Pathways is built with tangible interactions and visualizations on an interactive tabletop. The evaluation results of comparing Pathways with the current tools are presented in Chapter 6 and Chapter 7. The evaluation results support my hypotheses and suggest the new tangible interaction-based fitting process is more effective than the systems biologists' current tools.

3. **Design and development of large interactive tabletop displays to foster research projects**

The construction of the Tangible Tracking Table is shown in Chapter 4.1.1 and Appendix A. Some chosen applications built on TTT are illustrated in Chapter 4.1.2. The two interactive tabletops are still fostering new projects in Synlab.

4. **Remediation of a GUI-based game to tangible tabletop and observation of effects (Optical Chess)**

The design and development of Tangible Optical Chess is described in Chapter 4.2. The evaluation results and the impact to my later research are also included. The results encouraged my to design Pathways. Tangible Optical Chess is available on the tabletops in Synlab.

7.3 Generalizability and scalability

The results implicitly show that the combination of tangible interactions and visualizations is more efficient than the systems biologists' current tools, which largely depend on keyboards and mice to manipulate a lot of texts. I believe the encouraging evaluation results of Pathways do not apply to general problem solving cases. One reason is that the modelers don't have the tools to really understand what they are doing in a big picture sort of way - their approach is so fragmented that making discoveries / leaps of cognition is really hard. However, the subjective feedback from subjects showed that visualization (12 users' choice) and tangibility (3 users' choice) are two Pathways functions they liked the most. In addition, the evaluation shows Pathways is more effective than the systems biologists' current tools. These two results imply adding visual feedback to a tool that has no visualization could improve the efficiency of work. I believe Pathways could change the game in two possible fields; one is the simulation of computational models that require parameter adjusting, and the other is to control multivariate visualizations with tangible controllers.

One challenge of manipulating multivariate visualizations on GUI is to control all variables at the same time. Since these interfaces usually have one keyboard and once mouse, they are unlikely to provide intuitive multiple inputs. Tangible controllers on an interactive tabletop allow for multiple users and multiple inputs at the same time.

In the evaluation of Pathways, I created a predefined MAP kinase cascade model for the subjects to find the best solution. This model contained 4 enzymes, 8 molecules and 20 reactions. Among them, the 8 molecules and 10 reactions were dependent variables for the subjects to tune, and the rest were independent variables that remained constants all the time. Compared to a general real-world task, which involves at least 40 molecules, this is a relatively small model. Yet Pathways is able to adopt a model of that scale. It has built-in zoom, pan, and rotation functions that allow the user to concentrate on one part of the structure. The APIs are well documented and are flexible to create more complicated structures. In fact, the level of modeling complexity increases rapidly as the number of dependent variables increases. Pathways could be a better interface than the systems biologists' current tools for the users to tune one parameter and see its immediate effect.

7.4 Limitations and challenges

Pathways adopts the ODE model, which is a simple math model for simulating a pathway. There are many other math models systems biologists use to simulate biomedical reactions from different perspectives. Before Pathways includes more math models, its functionality will remain limited.

One of the many questions I got when demonstrating Pathways was, “Why not develop Pathways on iPad?” This type of question resulted, I believe, mainly from the fact that the current version of Pathways implements very simple tangible interactions that can be replaced with finger gestures or mouse interaction. Nevertheless, in the future, the tangible controllers can develop new forms of interaction that traditional input devices or touch screens cannot achieve. One example is the different versions of reactables [Jordà et al. 2007]. Reactable was first introduced as an interactive tabletop display [Jordà et al. 2007]. It allowed users to create music with tangible objects and finger touches. Some of the objects were cubes that had different functions on each of their sides. A user could rotate the cube to switch to a different function easily. When this type of tangible controller was implemented on a touch screen, the way users interacted with the interface changed, too. The challenge of creating a tablet version of Pathways will be to support the tangible interaction that is inherent on interactive tabletops or to invent a more effective interaction.

7.5 Applications of Pathways

Pathways was designed to use tangible interaction to simplify the complicated modeling tasks that systems biologists are currently working with. The evaluation results suggest that Pathways could be a faster method to provide approximate solutions to an abstract and highly complex problem. This could be very valuable in applications that are urgent. One of our subjects studied business in his graduate program. There are times when he has to configure an investment portfolio in one minute so that the configuration allows his customer to maximize profit in just one hour. For this type of problem, it can take longer than one minute to design a model for a computer program to solve it. If there is a tangible tool like this, he could find an investment portfolio with acceptable profits in a very short time. He explicitly pointed out that using the tangible dial to manipulate numbers is a “brilliant” idea – his words, not mine.

Ordinary Differential Equations (ODEs) describe the basic rules of many phenomena in nature. ODEs arise in many different contexts including biology, physics, and the social sciences. Visualization of an ODE helps learners to understand the characteristics of the equation. However, effectively visualizing a system of ODEs is more difficult, for the complexity of the ODEs makes them hard to comprehend. Moreover, it is difficult to see the effect of changing one parameter on a big ODE system. Pathways was designed to support biomedical modeling based on ODEs. In other words, Pathways visualizes ODEs in a way that allows users to be able to see the characteristics of the model better.

When Pathways is perceived as a visualization of ODEs, it can be used for visualizing several other biomedical reactions. For example, in the trafficking of macrophages from lung to lymph node and back, researchers want to know the number of macrophages in the lung and lymph nodes as time progresses. This reaction can be modeled with ODEs. ODEs can also be used to answer a question like this: “*How many tons of tuna can be harvested each year without killing off the population?*” To answer this question, I can write down the net rate of change of the tuna fish population in tons of tuna per year: *p’(t) = Birth rate – death rate - Harvest rate*. If we consider the food chain in the ocean, we can derive similar equations that represent the net rates of change for squids, mackerels, and sharks. As people increase the harvest of any of these fish, the whole chain changes. The whole set of ODEs, if implemented on Pathways, would be a more understandable interactive visualization. We can easily see if the number of one species would create an extreme change. The impact of over-harvesting any fish would cover all aspects.

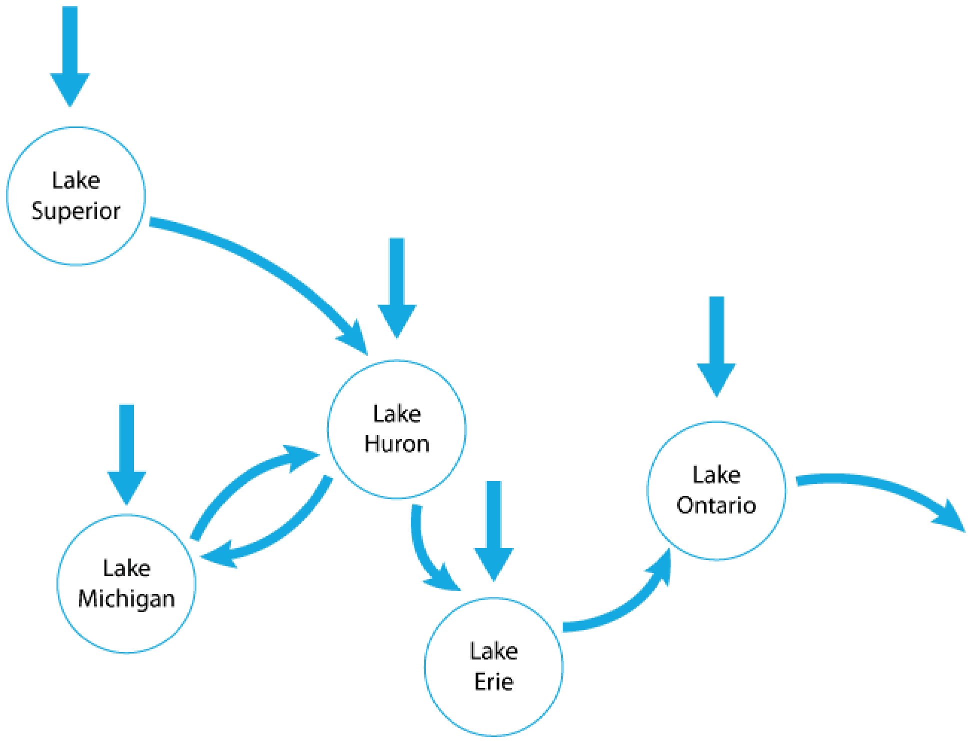


Figure 7-4 The network of waterways of the Great Lakes. The vertical arrows represent waterways from rain, rivers, and other sources.

Another possible application is the analysis of hydrologic cycles and water resources. The Great Lakes are connected by a network of waterways, which can be roughly depicted in Figure 7-4. This network of waterways can be used to create a hydrological model, which is described by ODEs. A Pathways like this can be used to determine the water balance of a region, mitigating and predicting floods, landslides, and drought risk or forecasting real-time floods, analyzing pollutants and natural solutes, or designing bridges and dams. What Pathways can provide is the real-time visualizations that reflect the changing of parameters. Actually, the Great Lakes idea is an appropriate application for the current version of Pathways since the waterways of the Great Lakes do not change as much as the structures in biomedical modeling. The model of the Great Lakes is fixed most of the time. Researchers can apply different weather conditions or solutes to see the simulation and influence in real-time.

7.6 Impacts

Changing the representation of data changes the way we are able to think about problems. While this is an accepted idea in the cognitive sciences, it is not well exploited in computational science where the problems are solved by algorithmic means. Since this project aims to change the way abstract scientific problems are represented using concepts from embodied cognition and embodied interaction, it opens up the possibility of finding solutions to problems that would otherwise take too long or seem too difficult to solve. Foldit has already demonstrated success in this area, but its impact is limited to structural problems. This thesis seeks to re-represent the larger class of more abstract scientific and engineering problems that are currently tackled by computational numerical methods. The Pathways system could also change the way researchers currently think about optimization algorithms and the way they are applied in discovery since Pathways applies embodied manipulation coupled with human visual-spatial skills. The project might also impact the nature of collaboration in biomedical modeling as it encourages several scientists to come together around a table and develop shared representations of problems.

Another possible impact is to science education. Since by re-representing abstract problems in a way that is understandable through our own embodied experience, we make it easier for students to comprehend them. Traditional lecturing methods are difficult to extend into inherently complex and interdisciplinary domains like biomedical engineering, and education in these areas needs to be rethought in ways that can help students think about problems at a higher level and from different perspectives (e.g. in biological, mathematical, or engineering terms). Although interactive tabletops have not yet achieved widespread use, an eventual tablet-based version of the modeling system could widen its near-term applicability to a broad range of educational contexts, including undergraduate and high school science education.

Embodied cognition is an important and growing area in cognitive science since we are now beginning to realize how closely actions done with the hands and body are linked to perception and imagination. This understanding requires us to re-think interface design. The evaluation results in this thesis support this notion by helping to establish embodied cognition as a framework for informing interaction design. It would also help to accelerate the design and use of interactive surfaces and embodied interaction in both science and education and in the design of control interfaces in multivariate visualizations. Pathways also helps us re-think information visualization from the perspective of embodiment and control mechanisms.

Pathways could also contribute to popular science by making abstract and highly complex problems accessible through embodied skills. The evaluation results show that non-systems biologists have accomplished satisfying results using the Pathways interface. They have accomplished even more after better understanding the problem. This has potentially significant impacts on the way science and engineering are practiced in society since it enables everyday citizens to engage with scientific and engineering problems and broadens participation in science and engineering by traditionally under-represented populations.

7.7 Future work

I imagine one possible next step of Pathways could be to connect the input and output with MATLAB or another visual modeling tool, e.g. the Cell Designer [Funahashi et al. 2008]. Cell Designer is a very versatile tool for modeling. What it lacks is the capability to quickly adjust the model and run the fitting tasks. If these two platforms are linked, systems biologists can use it to solve real world tasks by switching the modeling and fitting tasks between Pathways and Cell Designer. Also, the evaluation results suggest there is a potential that non-experts can perform the fitting tasks better than the experts. If the connection between Pathways and the systems biologists' current tools is established, systems biologists can focus on creating and editing the model, which require professional modeling knowledge. The fitting tasks can be assigned to non-systems biologists and only the best fitting solutions will be sent to the systems biologists for modifying the model. This is a process inspired by Foldit.

The questionnaire and subjective debrief results show that the tangible interactions and the visualizations contribution to the effectiveness of Pathways. However, there is no quantitative data to discover which one plays a more important role in the fitting process. To understand the effect of tangibility and visualizations, I will conduct more evaluations to compare TUI with GUI. In other words, users will face the same visual feedback while using different types of inputs. In one condition, tangible objects will be the controllers; in the other condition, a keyboard and a mouse will be the controller.

Because of the recent popularity of multi-touch tablets, I often got questions like "why not use finger gestures to control Pathways?" Adjusting numbers with multi-touch displays is a relatively new type of interaction to most people. Before these multi-touch devices have become prevalent, people used sliders, knobs, dials or buttons to enter numerical values. Which interface is a better to adjust numbers requires further study to find out.

Eventually, my collaborators and I will want to see the Pathways application work independently, meaning that it will be used to integrate the tasks of creating models, editing models, and fitting the results together. Moreover, Pathways could move to a more commonly adopted platform, e.g. a tablet computer. A user could select an element using her left index finger and rotate her mobile phone in her right hand to change the parameters. It is possible that tablets are not a replacement for tabletop, but another possible interface. For example, tabletop could serve as a public work area while tablets are used for individuals to enter private data.

7.8 Reflection

Most subjects recruited in the evaluation were graduate students from Georgia Tech. I did not evaluate the performance of teenagers or anyone over 40 years old. It will be interesting to see the evaluation of Pathways as people from a larger range of demographics use it since the younger generation might have more experience with the tangible user interface or interactive tabletops. Also, people who do not use computers often might find Pathways' interface friendlier than their experience with traditional desk or laptop computers. These postulations need more evaluations to support them.

I was pleased by the feedback that subjects gave indicating that they preferred Pathways' tangible interface over the other "current tools" interface, which was mainly GUI. However, this is not a comparison between TUI and GUI. One system biologist admitted that the representation of output charts in their current tools is not the best way to present then. He said that if he had the time and the right tools, he could design the same visualization on the MATLAB program. Because he is quite familiar with GUI, he thought he could perform on this new interface more effectively than on Pathways.

One of Pathways' goals was to support scientific discovery through tangible interaction and visualizations. However, the evaluation did not show much evidence that Pathways helps reveal the rules or trends of the model. Only one user (user0004) explicitly used the visualization to help him verify his hypothesis. The original evaluation plan was to conduct a cooperative think-aloud session when the user was performing the fitting task. I changed the evaluation plan to collect more quantitative data to substantiate my thesis claims. However, I would still like to see if Pathways could help further scientific discovery.

As I mention in Chapter 1.1, my vision of interface in the future is with physical objects augmented with digital/analog information in the physical space. Before the necessary technology was more accessible, I chose to realize this concept on interactive tabletop displays because the tabletops can provide the location sensing, visualizations, and other multimedia elements to enhance the physical objects on them. I also hope this thesis encourages more tangible user interface designs, especially TUIs combined with interactive tabletops.

Appendix A - Tangible Tracking Table Construction

The material needed for constructing a table includes:

Table A-1 Materials for constructing a tangible tracking table

Item	Description
IR Lamps	The wavelength has to match the IR filter's profile and the camera's sensor profile. To light up a 60" table, 6 to 8 lamps are essential.
Tracing paper	The tracing paper is used as a diffuser in front of the IR lamps to diffuse the IR light. It is also used as the projection screen placed on top of the tabletop.
Camera	A firewire (IEEE1394) camera is a better choice than a USB camera. A camera's sensor characteristic is very important. The sensor (either CMOS or CCD) has to be able to read light in the IR spectrum (about 850nm to 1000nm). Usually black and white cameras can detect more photons than color cameras in that range. A camera with at least 1024x768 resolution is necessary.
Camera lens	The lens has to match the type of the camera lens mount. After attaching the lens to the camera, be sure the camera can capture the whole tabletop. The lens should not have any filters on it.
IR filter	The IR filter will be placed on top of the camera lens. The profile of the filter has to match the sensor's profile of the camera and the wavelength of the IR lamps.
Cut IR filter	The cur IR filter will be places in front of the projector lens. It has to filter out the IR part of the light projecting from the projector and keep the visible light part.
Projector	A regular projector with 1024x768 resolution is ideal.
Tabletop	Usually an acrylic plastic sheet is sufficient. The thickness depends on the size of the tabletop. For a 36"x48" plastic, 0.5" is good enough to keep the surface stable.
Mirrors	Two front surface reflective mirrors. The size can be calculated in the next section.
Computer	A computer that can connect to the camera.
reacTIVision	The software is available here: http://reactivision.sourceforge.net/

The structure of the Tangible Tracking Table is shown in Figure 4-1. The detail construction blueprint is shown in Figure A-1 and Figure A-2. Before plotting this diagram, one has to measure the projection profile of the projector.

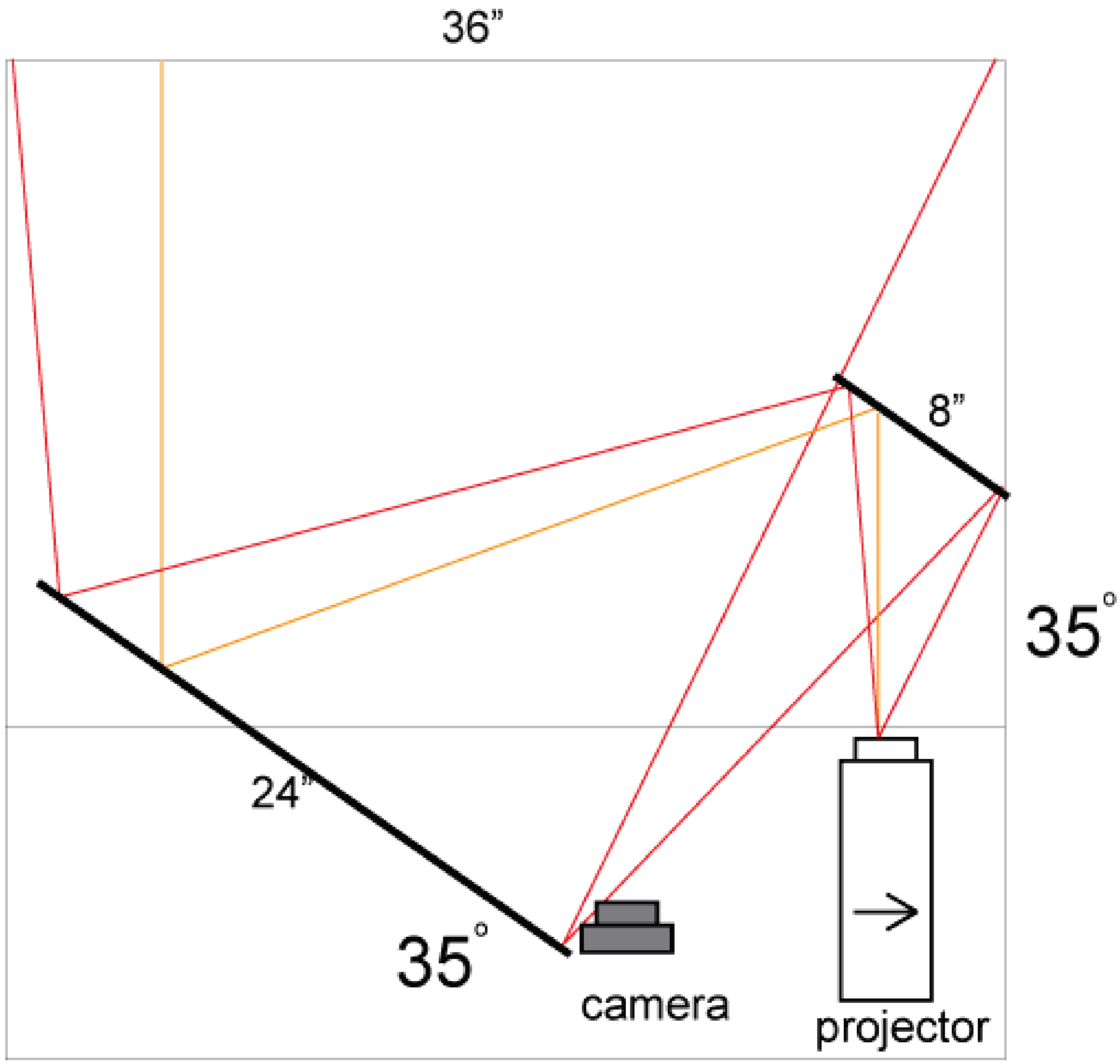


Figure A-1 The ray tracing diagram of the Tangible Tracking Table.

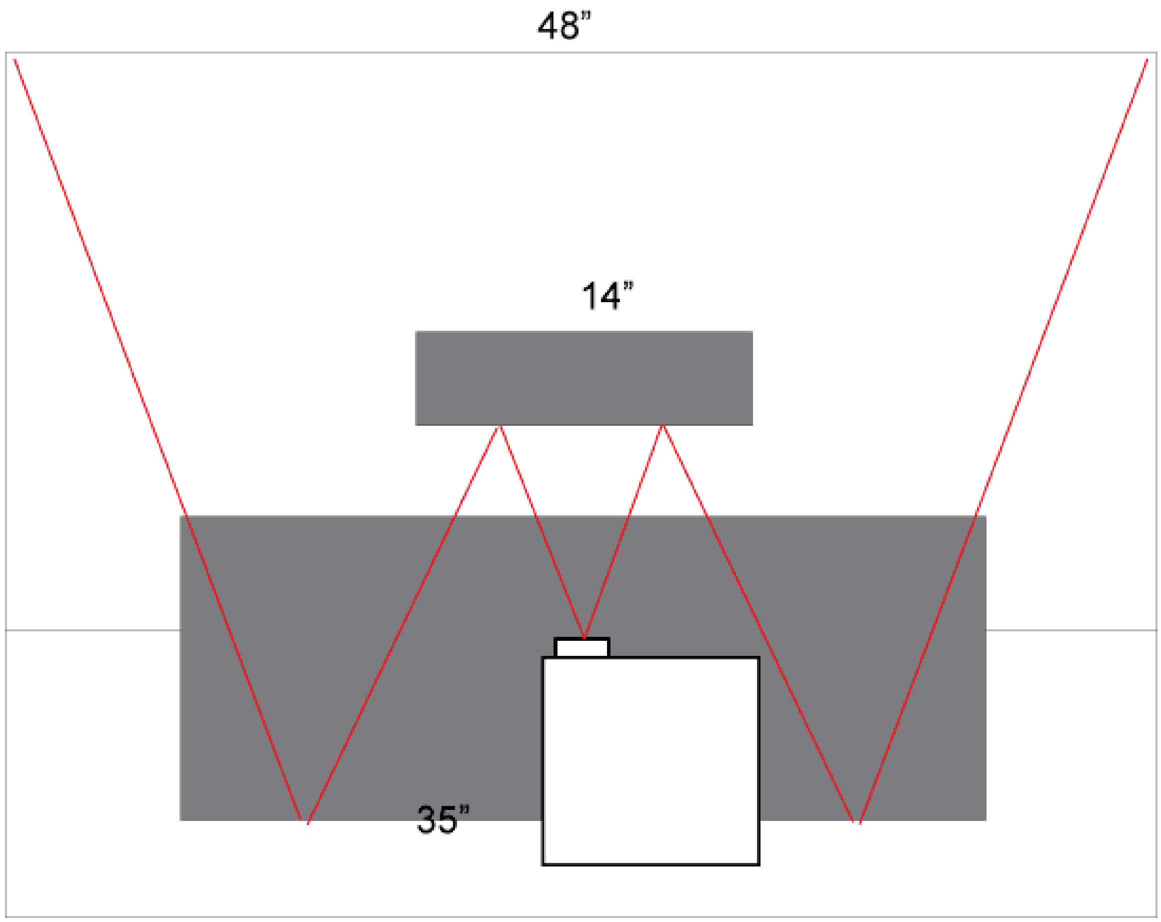


Figure A-2 The ray tracing diagram of the Tangible Tracking Table.

Appendix B - Pathways API Specification

B.1 API Description

Pathways API is built on top of the MT4j package. It uses third party libraries such as Processing's `core.jar`, `libTUIO.jar`, `TUIO.jar` and Flanagan's `flanagan.jar` [Flanagan 2012]. The Pathways API (application programming interface) specification is auto-generated in the doc directory of the Pathway package.

Log files are stored in `log/`.

The configure file of Pathways is `/pathways.config`. The configure file of MT4j is `Settings.txt`.

B.1.1 Packages

There are 6 main packages listed here. The three classes in bold font are the user-defined classes that are fundamental to run a Pathways application.

`edu/gatech/synlab/pathways`:

`ChartSet (class to generate all output charts and the chart controller)`

`NumberController (class to create the dial controller)`

`PathwaysScene` `(the class for the pathways scene)`

`StartPathwaysScene` `(the main class)`

`edu/gatech/synlab/pathways/components`:

`BezierLink (class to create the visual link between the dial and the selected element)`

`LineChart (class to generate one output chart)`

Molecule (class to generate one molecule)
RadarChart (class to generate one radar chart)
Reaction (class to generate one reaction)

edu/gatech/synlab/pathways/components/shapes:

Baseline (class to create the moving time line on the chart)
MovingArrow (class to generate one animated reaction arrow)
PathwaysBezier (class to create Bézier curves)
Radar (class to create the radar chart)

edu/gatech/synlab/pathways/processing:

(the second Pathways prototype in Processing)

edu/gatech/synlab/pathways/util:

Counter (class to create the time counter)
CounterCallback (interface to create the time events)
MathTools (some math functions)
SetupManager (load the setup file)
TuioLogger (save all TUIO event in a log file)

edu/gatech/synlab/pathways/util/math:

MAPKinaseCascade (the user-defined ODE)
ODESolver (class to solve ODE)
ODEs (class to solve ODE)
RungeKutta2 (class to solve ODE using the Runge Kutta method)

B.2 Usage Instructions

To create a new Pathway application that simulates the Great Lake waterways illustrated in Figure 7-4, follow the step-by-step instructions:

Step 1. Create a file that setup the scene, e.g. **`GreatLakeScene.java`**

The file should define all molecules (lakes), reactions (all water flows), the output chart, the dial controller and the radar chart. Also create the main Java class, e.g. **`StartGreatLakeScene.java`**. Add some other components to the scene if necessary, e.g. time counter, a custom setup file, or the TUIO logger.

Step 2. The scene has to implement `IMTInputEventListener`

`GreatLakeScene.java` has to implement `IMTInputEventListener` to create any tabletop interactions. There's one method: `public boolean processInputEvent(MTInputEvent inEvt)` in this interface. To define the tangible interaction, the method has to handle three fiducial input evnets:

MTFiducialInputEvt.*INPUT_STARTED*, MTFiducialInputEvt.*INPUT_UPDATED*, MTFiducialInputEvt.*INPUT_ENDED*.

Step 3. Create a file that describes the ODEs, e.g. **`Waterway.java`**.

It has to implement `flanagan.integration.DerivnFunction` and `ODEs`. It should also define `double[] derivn(double x, double[] y)`, which defines the ODEs for this project.

B.3 IRB Protocol

B.4 Overview

Designing Tabletop Visualizations to Support the Fitting Process in Systems Biological Modeling

In this document, we outline the “Pathways” user study. “Pathways” visualizes the simulation of bio-chemical networks using a Tangible User Interface (TUI) approach. By adopting TUIs for visualization, we believe that researchers will be able to manipulate these parameters more easily, and also see the system-wide effects of their manipulation across the reaction network.

Introduction

We are interested in observing how kinesthetic interactions improve the way we think about and solve problems in computational simulations.

Main Objectives

Currently in systems biology, researchers run simulation programs that model different experimental parameters such as concentrations inside cells and reaction speeds. These parameters are adjusted to discover hidden patterns in the reaction network, often by plotting the output using graphs. Our attempt is to visualize the reaction network on an interactive tabletop display. Researchers control the parameters with tangible objects and their hands, allowing them to change parameters in a continuous fashion, and focus on understanding the effects of this manipulation, rather than on programming or entering numerical values. Our research question is, "*does tangible and embodied interaction improve the way we think about and solve problems in computational simulations?*"

Methods

We will recruit participants from Georgia Tech. We will describe our research project and ask them to go through the consent form to see if they want to attend the study. If they agree to participate, we will make an appointment at TSRB to conduct the study.

Since Pathways is designed to improve the efficiency of the fitting process in systems biological modeling, our subject sets will mainly consist of systems biologists. However, we also plan to recruit subjects from other backgrounds, who see Pathways as a tool with potential to solve other complicated problems in their respective areas (e.g. supply chain optimization problem) in the future.

We plan to recruit a total of 36 participants. The study will begin with a 5-minute consent.

- For subjects with bio-chemical modeling background:
    - a 10 minute semi-structured interview will follow, which will focus on current modeling practice.
- For other subjects:
    - a 5 minute semi-structured interview to obtain their background information.
- Later, we will counterbalance the subjects. Half of them will be assigned to perform the task on GUI system first.

   - There will be 10 minutes allotted for the subjects to familiarize with the system, where they will also be introduced to the system conceptually.
   - The subjects will then be asked to perform one fitting task on GUI.
- Once finished with GUI, subjects will be asked to perform the same task on the Pathways prototype.
   - There will also be 10 minutes allotted for the subjects to familiarize with the system, where they will also be introduced to the system conceptually.
   - The subjects will then be asked to perform one fitting task on GUI.
- At the end of the study, we will ask the subject to give a 10 minute Likert scale questionnaire and subjective debrief.
- Total time for study will be 65-75 minutes.

The whole process will be videotaped. We will erase the video records once the analysis is complete. (The video will not be displayed publicly)

B.4.1 Study 1 – Exploratory research

5 minute consent

System Biologists:

10 minute semi-structured interview

Questions to be asked:

1. We'd like to begin by asking you to tell us a little bit about how do you model a bio chemical reaction?

2. How long have you been modeling? Do you consider yourself a beginner, an intermediate or an expert?

3. What tools do you use? (Pen, paper, software, computer, multiple monitors)?

   How and when do you use them?

   - Pen
   - Paper
   - Software
   - Computer
   - Multiple monitors/ large screen
   - Others

4. Usually how much time does it take to complete a model? What about to find a fit solution?

5. Do you visualize your model or your output?

   Can you show me an example?

6. How do you compare your simulation data with the experiment data?

7. Do you collaborate with others?

8. Are there any other thoughts about modeling or the fitting process?

9. Have you ever used an interactive tabletop before? (where? Which tabletop? What application?)

Non-System Biologists:

5 minute semi-structured interview

Questions to be asked:

1. Do you write computer programs?
2. Have you ever used an interactive tabletop before?

B.4.2 Study2 – Acceptance test, usability testing

10 minute introduction & get familiar with the systems

20 minutes tests

Tasks:

Given a set of test data and a predefined model, change the parameters of the initial concentrations to fit the test data

The subject will finish the task on two different interfaces; each of them will take 10 minutes for introduction and 10 minutes fo performing the tasks.

10 minutes Subjective Debrief (subjective: subjects' feelings about the experience)

B.4.3 Study 3 – Subjective Debrief

Table B-1 Questionnaire

		Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
1	The tabletop visualization makes fitting process easier comparing with the graphical user interface version.					
2	I could see myself using the Pathways system					
3	Using tangibles to control the values is efficient.					
4	Visualization is not distracting					
5	The visualization could improve my work or make me better understand the model, the molecules, the reactions and the relationships between them					
6	**[Systems Biologists only]** This new fitting process is more effective than my current method.					

Follow-ups

(3 minutes)

1. The tabletop visualization makes fitting process easier than that using GUI version.

Follow-up: tell us more about your choice (why did you make that particular choice?).

Probe: would you use it for demonstration or solving real tasks?

Probe: What would be a barrier to you using the system?

Other Questions

(5 minutes)

1. What did you think was the best feature of the system?

2. Is there any feature missing that you would have liked to see included?

Probe :

[Systems Biologists] To hide/show numbers or ODEs?

option settings? save/edit? visualization? Sound feedback?

3. What fitting strategies did you use on the GUI system? Did you fit the graphs or the RMS error values?

4. What fitting strategies did you use on the TUI system? Did you fit the graphs or did you use the radar chart to help you?

5. Any other thoughts you would like to share?

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